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SURGICAL TREATMENT OF DIVERTICULITIS OF THE COLON

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Facts potentially useful in the diagnosis and treatment of diverticulitis of the colon were sought in a study of 70 patients in whom that condition was found at operation. Forty were men, and the youngest patient was 39 years old. In 16 the symptoms were acute; in 19 there had been intermittent trouble for years. Symptoms varied, and there were 18 patients in whom none of the symptoms was gastrointestinal. In 14 the preoperative diagnosis had been neoplastic disease of the intestine or pelvic organs. Leukocytosis was present in only half of the patients; the same was true of fever. Gross bleeding occurred in 13. Roentgenologic examination did not always distinguish between presence and absence of inflammatory changes, and in 11 instances the radiologic report was decidedly misleading. In 62 patients the lesion involved the sigmoid colon; in 35 of these it was treated by primary section and anastomosis. The experience of the authors with this operation has been favorable, and they urge that it be carried out, when appropriate, before serious complications can develop.

MOST studies of diverticulitis of the colon come from the large teaching centers. Their leadership in developing a more aggressive and radical approach to the problem is well recognized. No longer is surgical treatment carried out as a last resort, as a lifesaving measure, or only when dire complications develop.[1] There is an increasing trend toward offering it early to patients failing to respond to medical treatment.[2] In addition, since the advent of antibiotics and chemotherapeutic agents, an attempt usually is made to remove the diseased segment and not simply to bypass it.[3] Stage operations are seen with ever-decreasing frequency and with progressive shortening of the interval between stages.[4]

Material and Methods

Records of all patients operated on for diverticulitis of the colon at Sacred Heart Hospital from Jan. 1, 1951, to Dec. 31, 1957, were reviewed by us. No attempt at long-term follow-up was made as we were principally interested in accuracy of diagnosis, procedures carried out, and postoperative complications. Seventy patients provided the basis for this study.

Principal locations of the inflamed diverticula were the cecum in 5 patients, transverse colon in 2, entire colon in 1, and sigmoid colon in 62. Since the active disease process which led to operation was confined to the sigmoid colon in the vast majority of patients, it is this group to which closest attention has been paid in this study.

There were 40 men and 30 women. The youngest patient was a man aged 39 with a perforating cecal diverticulum, the oldest an 87-year-old man with

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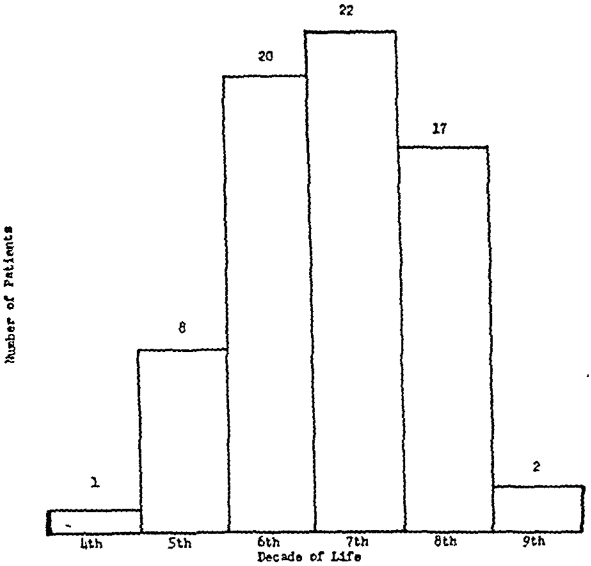
From the Rockwood Clinic.

perforating sigmoid diverticulitis. The distribution of patients according to age is shown in the figure.

Symptoms

In patients whose involvement was in segments of the colon other than the sigmoid, symptoms were, with one exception, acute and of a few hours' to a few days' duration. Patients with sigmoid diverticulitis exhibited considerable variation in the duration of their symptoms. In 16 patients symptoms were acute and measured in terms of hours or days. In 13 patients duration was measured in weeks, in 11 it was measured in months. Nineteen patients had had intermittent trouble for years, manifested in some by vague, ill-defined complaints and in others by recurrent, acute flare-ups often requiring repeated hospitalization. Three patients had no symptoms to suggest the condition, which was discovered at operation.



Age distribution of 70 patients with surgical treatment of diverticulitis of colon.

In patients with lesions of the cecum and transverse colon the uniform complaint was pain localized to that portion of the abdomen containing the disease process, with the exception of one patient with a transverse colon lesion whose symptoms were obstructive in character. One patient with involvement of the entire colon was admitted because of a massive gastrointestinal hemorrhage. Forty-nine of the 62 patients with sigmoid diverticulitis complained of pain, but definite localization was less constant. Other complaints were of constipation, 16, with obstipation in 5; diarrhea, 8 patients; and nausea and vomiting, 7 patients. Thirteen patients had noted the passage of bright blood per rectum; in 9 this was of some magnitude, but in only 4 was it associated with anemia. Four of the patients who had bled had no other complaints whatsoever. Seven patients gave a history of chills and/or fever. In five patients bladder symptoms were predominant. A few patients complained of bloating, weight loss, and general indisposition. Eighteen patients had no symptoms whatsoever referable to the gastrointestinal tract.

Findings

The five patients with cecal lesions had tenderness localized to the right lower quadrant; four had fever; and a mass was noted in one. Both patients with transverse colon lesions had tenderness over the lesion; in one, a mass was palpable. No findings, except pallor, were noted in the 78-year-old man with diffuse involvement of the colon. Two of the patients with ascending colon lesions exhibited leukocytosis. All but two of the foregoing patients were anemic. Four patients had had barium enemas carried out with the following diagnoses: diverticulosis, one; carcinoma of the transverse colon, one; polyp of the cecum, one; ileocecal intussusception, one. Thirty-eight of the 62 patients with sigmoid diverticulitis exhibited lower abdominal tenderness, most marked in the left lower quadrant. In 19 patients a mass was palpable. Fifteen patients exhibited varying degrees of distention. Six were febrile on admission. One patient developed an abdominal wall fecal fistula shortly after admission. Two patients had such fistulas at the time of admission and in one of these patients it was associated with a clostridial wound infection. Two patients had colonic stomas when first seen. In 13 patients no abnormal physical findings were reported.

In 21 of these patients varying degrees of anemia were present, and 31 had elevated leukocyte counts on admission. Proctoscopic examination was carried out in 25 patients, with positive findings in 13. In three patients this consisted only of the presence of blood coming from the upper reaches of the intestine, whereas in the remainder evidence of inflammation and occasionally the presence of diverticula were noted. A plain film of the abdomen was made in 10 patients with the following diagnoses: abdominal mass, 1; intestinal obstruction, 5; negative, 4. A barium enema was carried out in 46 patients with the following diagnoses: diverticulitis, 27; diverticulosis, 10; carcinoma, 3; constricting lesion, 3; extrinsic tumor, 2; and negative, 1. In two of the patients in whom radiologic diagnosis of diverticulitis was made, the possibility of a carcinoma could not be excluded. Among the 11 patients in whom the diagnosis was "diverticulosis" or "negative," 8 were found at operation to have severe, active diverticulitis.

We were interested in learning what the clinician thought he was dealing with before the patient was operated on and also in the accuracy of the surgeon's assessment of the findings at operation. Preoperative diagnoses are shown in table 1. No correct ones were made in patients having lesions of the cecum or transverse colon. Although the condition was known to exist throughout the entire colon in the patient ultimately undergoing colectomy, the source of the bleeding was incorrectly inferred and a hemorrhoidectomy carried out first. Among patients with sigmoid lesions a correct diagnosis was made or strongly suspected in 61%. One of the patients on whom a correct preoperative diagnosis was made here entered the hospital with a fecal fistula and a clostridial wound infection resulting from an operation carried out elsewhere on what was thought to be a strangulated inguinal hernia, six days previously.

Table 1.—*Preoperative Diagnosis in Seventy Patients with Diverticulitis*

Location of Lesion	Diagnosis	No.	% Correct
Cecum	Acute appendicitis	3	0
	Carcinoma	2	0
Transverse colon	Strangulated periumbilical hernia	1	0
	Carcinoma	1	0
Entire colon ..	Diverticulitis	1	100
Sigmoid colon	Diverticulitis	29	61
	Possible diverticulitis	9	
	Carcinoma	7	
	Gynecologic disease (ovary 6, uterus 1)	7	
	Acute appendicitis	5	
	Unknown or incidental finding	5	

At the time of operation the correct pathology was recognized by the surgeon in three patients with cecal lesions; in two he thought he was dealing with a carcinoma. The true nature of the condition was apparent in the patients having lesions of the transverse colon and entire colon. Among the patients with sigmoid lesions a correct assessment was achieved in 85%. In four patients the lesion was thought to be carcinoma, while in five the surgeon was uncertain as to the nature of the lesion with which he was dealing.

Treatment

Operative procedures which were performed are indicated in table 2. Among the patients with cecal lesions, right hemicolectomy was carried out in two patients because the lesion was thought to be malignant and in the third because of the extent of the process. Local procedures were utilized when the inflammatory nature of the process was obvious and circumscribed. In both patients with transverse colon lesions, the inflammatory nature was obvious and the extent of the process dictated whether resection or excision was performed. The patient with extensive involvement of the entire colon underwent subtotal colectomy after an ill-advised hemorrhoidectomy failed to curtail his bleeding.

Sigmoid diverticulitis was treated by primary resection and anastomosis in 35 patients. None of these patients had complementary cecostomy or colostomy performed. In only eight patients was the pathological process quiescent at time of operation. In 20 patients marked inflammatory activity was present and 2 of these patients were partially obstructed. In six seriously ill patients abscesses were encountered, and in one patient acute perforation with generalized peritonitis was present.

Stage procedures were carried out in 14 patients. In one instance complementary colostomy was established because of an uncertain anastomosis. In two instances the presence of a large abscess and in one the presence of a clostridial wound infection were the reasons for stage procedures; two of these patients had associated fistulas, as did one other patient in whom a stage procedure was carried out. In five patients the presence of obstruction in a poor-risk patient with active disease was the indication for preliminary decompression. In three instances the true nature of the process was wholly unsuspected, no preparation for an intestinal operation had been carried out, and it was felt unwise to proceed with a primary resection; two of these patients were operated on with a diagnosis of "acute abdomen" and the third because of a mass. The final patient had a ruptured diverticulum, generalized peritonitis, and a gallstone impacted in the terminal ileum.

In four patients local procedures were carried out: in one instance this was done in association with a salpingo-oophorectomy in an effort to relieve low-grade obstruction; in one, after appendectomy, to remove a piece of bone protruding from a perforated sigmoid diverticulum. It was hard to explain the surgeon's choice in the other two patients, in both of whom diverticula were removed, once because of acute perforation and once in association with colporrhaphy and hysterectomy.

Transverse colostomy was performed twice, once in an 87-year-old man with perforation and peritonitis, and once in a 75-year-old critically ill man with severe cardiovascular disease who had obstruction due to his diverticulitis and hemoperitoneum from a bleeding hemangioma of the liver. In the remaining seven patients with sigmoid diverticulitis, although the process was recognized at operation, no procedure conducted directly against it was carried out. In two instances pus was encountered and drainage instituted. Four times diverticulitis was discovered in the course of other operative procedures and because of lack of preparation or history of adequate medical care, a conservative course was elected. In one case when coloscopy failed to reveal the source of bleeding from the intestine, the abdomen was closed and the patient's hemorrhoids removed.

Table 2.—*Surgical Treatment of Diverticulitis in Seventy Patients*

Segment of Colon Involved	Operative Procedure	No. of Patients
Cecum	Right hemicolectomy	3
	Excision and appendectomy	2
Transverse colon	Resection transverse colon	1
	Local excision	1
Entire colon	Subtotal colectomy	1
Sigmoid colon	One-stage resection	35
	Multiple-stage resection	14
	Local procedure	4
	Colostomy only	2
	Exploration	7

In all cases in which tissue was removed the pathologist confirmed the diagnosis of diverticulosis or diverticulitis. In one patient a 3 mm. sessile polyp also was found to be present, and in another a grade 2, Duke's A adenocarcinoma 1 cm. in diameter was found to be present in the removed sigmoid segment.

Postoperative Course

The postoperative morbidity and mortality are given in table 3. One of the five patients with diverticulitis of the cecum developed mild femoral thrombophlebitis, and one developed a large wound hematoma. The convalescence of the remaining three was uneventful. Both patients operated on for diverticulitis of the transverse colon had an uneventful convalescence. The patient who was operated on for diverticulitis of the entire colon developed an infected wound hematoma and a severe transfusion reaction complicated by jaundice. Among the 35 patients undergoing one-stage resection for diverticulitis of the sigmoid, complications occurred in 7. In one instance the left ureter was injured in the process of mobilizing the acutely inflamed sigmoid; fortunately, the injury was noted at the time of operation, repaired over a T-tube, and caused no further trouble. One patient went into shock postoperatively. One patient was thought to have developed a leak in the anastomosis; the process responded well to conservative therapy. There was one instance of ileus and one of small intestine obstruction, both of which responded well to conservative measures. One patient developed transient auricular fibrillation. One patient had to be readmitted because of a mild wound dehiscence. A number of patients were troubled with transient diarrhea and weight loss, but in none did this persist or become a serious problem. Transient mental depression and confusion were occasionally noted in the immediate postoperative period.

TABLE 3.—*Morbidity and Mortality Among Seventy Patients Operated on for Diverticulitis*

Segments of Colon Involved	No. of Patients	Patients with Post-operative Complications	Deaths
Cecum	5	2	0
Transverse colon	2	0	0
Entire colon	1	1	0
Sigmoid colon:			
One-stage resection and anastomosis	35	7	0
Multiple-stage and other procedures	27	10	2

Among the 14 patients having stage procedures there was one death. This occurred in a 78-year-old woman on whom a colostomy was performed for acute perforation of a sigmoid diverticulum with generalized peritonitis and in whom an impacted gallstone had to be removed from the ileum at the same time. Three weeks later the diseased segment of the sigmoid was resected. Postoperatively she developed congestive heart failure, the anastomosis leaked, generalized peritonitis developed, and she finally died of a pulmonary embolus on the seventh postoperative day. Complications among the remaining patients included two instances of severe wound infection with abscess formation, one of recurrent fistula, one of small intestine obstruction, one of gangrenous cholecystitis, and one of prolonged urinary retention. Shock followed closure of colostomy in one patient, and another had an unexplained fever for some time. Again diarrhea was occasionally troublesome in the postoperative period. In two of the patients undergoing local procedures recovery was uncomplicated; the course of the other two was febrile, in one associated with the development of a large abscess. Of the two patients on whom transverse colostomy was performed, one, aged 75, died on the 33rd postoperative day of pneumonia which followed atelectasis. The other, aged 87, recovered uneventfully. In those patients in whom nothing was done about the diverticulitis per se at the time of operation no complications occurred, with the exception of one patient who had prolonged urinary retention and syncopal episodes.

Comment

When this clinical study was initiated, we had in mind several questions in regard to the diagnosis and management of diverticulitis, the answers to which we felt were not clear. We do not have a complete answer to each of these questions; nevertheless, we feel justified in presenting certain facts from which, in our opinion, a number of conclusions may be drawn. Diverticulitis, in portions of the colon other than the sigmoid, occurred with such infrequency that it would seem unjustifiable to do more than call attention to the fact that it does occur and is seldom diagnosed before operation.

To discuss the diagnosis of sigmoid diverticulitis might seem elementary, yet we were astonished to find that this diagnosis was not even considered by either clinician or surgeon prior to operation in 39% of the cases we reviewed. An analysis of the reasons for faulty diagnosis brings out the following significant points:

1. Diverticulitis frequently presents a clinical picture mimicking gynecologic disease or carcinoma of the intestine. Others [5] have adequately emphasized concern as to avoiding the pitfall of mistaking sigmoid carcinoma for diverticulitis. To this we heartily lend support, yet in our group of patients no such error was made. Instead, in 14 cases neoplastic disease of the intestine or pelvic organs was the sole preoperation impression, gained, it seems, as the result of a mass being palpable in the lower part of the abdomen or on pelvic examination and in the absence of signs of inflammatory disease. We would urge, as have Bacon and Sherman,[6] the inclusion of sigmoid diverticulitis in the differential diagnosis of such a mass regardless of its size and the absence of local tenderness or systemic evidence of inflammatory disease.

2. In contrast to the above, diverticulitis coli, complicated by perforation, may mimic diseases which produce generalized peritonitis, in particular, appendicitis. Careful clinical examination should help to minimize this mistake, as should keeping in

mind the fact that perforating sigmoid diverticulitis can present abdominal signs elsewhere than the left lower quadrant, as Fallis and Marshall[7] have pointed out.

3. An absence of significant aberration of lower gastrointestinal function should not lead to the exclusion of acute sigmoid diverticulitis from the differential diagnosis. In 18 of our cases (30%) a change in bowel habit had not occurred or was so slight that it seemed insignificant. Colcock[5a] states that 35% of his patients had a change in bowel habit, implying that as many as 65% had no such helpful diagnostic symptom. This is in contrast to Judd and Mears,[8] who report that only 2 out of 68 surgical cases of diverticulitis had no bowel symptoms.

4. Leukocytosis is as frequently absent as it is *present in acute diverticulitis of the sigmoid colon*, according to our study. This surprising finding is another factor urging us to call attention to the frequency of the noninflammatory character of the clinical picture in many patients. Of the 32 patients in our group whose white blood cell count was 10,000 per cubic millimeter or under, many were acutely ill, and, whereas diverticulitis was diagnosed in most, in 12 of this group it was not suspected.

5. Fever was absent as often as present in patients with acute diverticulitis.

6. Bleeding from diverticula or as a symptom of acute diverticulitis coli has received a good deal of attention in the literature. Gross bleeding was noted by 13 of our patients, but was only one symptom among many except in 4 patients in whom it was the sole presenting complaint. Massive hemorrhage was the chief cause for surgery in two of these patients. Certainly gross bleeding should first of all suggest a disease of the intestine other than diverticulitis. When it does arise from diverticula, it frequently makes the diagnosis extremely difficult.

7. A report from the radiologist indicating the presence of diverticulosis of the sigmoid without evidence of diverticulitis does not mean that significant inflammatory changes are absent. This discrepancy should be recognized by all clinicians and is one of the pitfalls of blind belief in the infallibility of x-ray examination. In 11 instances in our group of patients the radiologic report was decidedly misleading.

We have made no comments concerning the type or location of pain suffered by these patients, inasmuch as we were unable to note any pattern of distress that has not been fully discussed elsewhere. Insofar as treatment is concerned this study deals only with patients operated on. The reader is directed elsewhere for a detailed discussion of indications for operation. Among our patients the indications were, in order of frequency: intractability of symptoms, the presence of a palpable mass, the inability of the radiologist to exclude carcinoma, obstruction, bleeding, and external fistula.

Surgical Procedures.—Surgical procedures may well be considered in three catagories: (1) the elective operation, (2) the emergency operation, and (3) the surprise operation.

When operation is carried out as an elective procedure during a quiescent phase of the disease there is general agreement that a one-stage resection and anastomosis is the procedure of choice.[8] Resection can usually be limited to the sigmoid even though diverticula may be scattered throughout other parts of the intestine. In only one of our patients was it necessary to carry out a subtotal colectomy. In the more complicated case there is no such unanimity of feeling. It is our feeling that a phlegmonous process in the intestine wall, with or without miliary abscesses and extensive local adhesions, low grades of obstruction, severe bleeding, *and fistula do not render a multistage procedure* mandatory. It should be the condition of the patient rather than the local findings which influences the decision. If the patient is in good general condition and well prepared, it is usually possible to get above and below the diseased segment to achieve a satisfactory anastomosis of comparatively normal intestine. The more radical procedure is sometimes the safer. By adequate mobilization and resection one removes all diseased tissue, avoids tension on the anastomosis, and eliminates the need for subsequent operations with their attendant risks, time loss, and expense. This was the policy followed in 35 of the 62 patients having sigmoid diverticulitis and 5 of the 8 patients with diverticulitis in other portions of the colon. There were no deaths in this group; complications were less frequent and for the most part comparatively trivial.

In the presence of high grades of obstruction, when a large abscess is present which cannot be removed without profound soiling of the peritoneal cavity and leaving behind much devitalized tissue, or when the patient's general condition is poor, obviously a staged procedure offers the only safe approach to the problem. A transverse colostomy will usually allow the inflammatory process to quiet down and keep it quiet as long as the stoma is functioning. This alone may be all that can be done in an extremely poor-risk patient and may offer excellent palliation as far as the diverticulitis is concerned. It is interesting to note that one of our two deaths occurred when a colostomy alone was performed. After recovery from the colostomy, at an interval of two weeks to several months, the diseased segment of intestine may be removed whenever the patient's general condition warrants. If the resection and anastomosis are easily accomplished, many times the colonic stoma may be closed at the same time. If the procedure is difficult, the condition of the intestine leaves much to be desired, and the patient's general condition is poor, closure should be carried out as a third stage. Our only other death occurred in a poor-risk patient in whom multiple severe complications followed a staged procedure. In general, complications were more frequent and severe in this group of patients.

We were surprised to find a few local procedures still being carried out. In the ascending or transverse colon this may occasionally be adequate. In the sigmoid, where multiple diverticula usually exist, it is difficult to justify attempts to remove individual diverticula. Pemberton and co-workers[3] long ago decried the practice as seldom conducive to lasting relief from disease. Similarly, in two cases with localized peritonitis and abscess, drainage alone was carried out. Both patients survived but in neither, of course, was the basic problem solved.

When acute perforation occurs with spreading or generalized peritonitis, the need for emergency operation is unquestioned, but as to procedure the decision may be difficult. Although acute perforation occurred in four of our patients, it is not common. Pemberton and co-workers[3] reported no instances of acute perforation in 389 cases of diverticulitis. Mayo and Blunt,[9] discussing complications of diverticulitis, found abscess in 57 of 202 cases but no free perforation. Fallis and Marshall[7] reported five deaths with conservative treatment of acute perforation. Exteriorization or extraperitoneal resection would seem to be the logical procedure. However, it is seldom feasible as the mesentery is often short and thick and all the affected intestine cannot be safely brought to the outside. In general, closing or patching with omentum of the perforated diverticulum is the procedure of choice, although sometimes only drainage can be carried out. Needless to say, a transverse colostomy always should accompany procedures of this type. Closure or drainage without complementary colostomy offers questionable security.

Since accurate diagnosis at operation is particularly difficult in the presence of acute perforation, subsequent resection should be carried out not only to remove the diseased intestine but also to avoid the disaster of leaving a carcinoma behind. Immediate primary resection and anastomosis may be done if the patient is seen early and conditions are favorable. Unfortunately, this seldom is the case, but in one of our patients it was done with an eminently satisfactory result.

The surprise operation is performed with distressing frequency. This situation prevails when the first intimation of the correct diagnosis is obtained after the abdomen is opened. Because of lack of proper conception of the problem, the usual routine preparations which have added so much to the safety of elective intestinal surgery have not been carried out. The actual operation finds both the surgeon and the patient unprepared for what should be done. Sometimes, as in the presence of perforation, abscess, or obstruction, the surgeon has no alternative but to proceed boldly and hope for the best. However, in the presence of uncomplicated diverticulitis, be it fulminating or quiescent, a dilemma may present itself. In seven patients in our series the surgeon elected to correct any associated lesions and back out, planning to give the patient a trial of adequate medical therapy and then, if necessary, to reoperate and resect the diseased intestine under more favorable circumstances. However, in most cases where the disease was pronounced, the surgeon faced his problem resolutely and attempted some type of definitive procedure. One can only hope that periodic references to this disease in the literature will serve as a reminder of the frequency of its occurrence and keep "surprises" at a minimum.

Summary

Diverticulitis of the colon is a common condition frequently necessitating surgical treatment. It must be considered in the differential diagnosis of intra-abdominal disease, especially if an abdominal or pelvic mass is present, regardless of the absence of localized or generalized signs of inflammation and regardless of an x-ray report of diverticulosis instead of diverticulitis. In an increasing number of patients the surgical treatment of choice is one-stage resection and anastomosis. In the present series of 70 patients this was carried out in 57% of the total patients with diverticulitis and in 71% of the patients with sigmoid diverticulitis undergoing definitive surgery, with no deaths and minimal morbidity. No longer should this procedure be reserved merely for the uncomplicated or quiescent cases. If recognition and treatment are delayed until serious complications develop, multiple-stage procedures may still have to be carried out.

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SURGICAL MANAGEMENT OF ULCERATIVE COLITIS

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Surgical treatment becomes necessary in a certain number of patients with ulcerative colitis who do not respond to medical management. The operation of low ileorectal anastomosis here described is done a year or more after subtotal colectomy and ileostomy. It consists in mobilizing the rectum, excising part of the rectum with the sigmoid colon, and making an end-to-side anastomosis of ileum to the remaining part of the rectum. During the first few weeks after the second stage, frequent defecations caused considerable disability, but this generally subsided. In 13 patients rectal continence was attained after the first several defecations after the ileoproctostomy; in the remaining one patient incontinence persisted because the sphincter had been damaged by years of preoperative disease. In all cases the anastomosis healed without formation of abscess or fistula. This operation should be considered whenever the rectum and its sphincter mechanism have escaped serious damage, since it offers the hope of avoiding a permanent ileostomy.

The medical management of chronic nonspecific ulcerative colitis is the province of the gastroenterologist. The judicious use of steroid therapy, blood transfusions, certain sulfonamides, and diet under hospital supervision has resulted in satisfactory arrest of the disease in 80% of patients with ulcerative colitis. Surgical management is reserved for those who do not respond to medical therapy. In past years the incalculable morbidity attending the surgical treatment of this disease has led gastroenterologists to defer surgery and to prolong medical treatment despite hopeless odds. This rigid attitude is now being softened by a marked reduction in morbidity that may be attributed to the practice of two principles: "removal of the disease" and construction of a physiological ileostomy.

The absolute indications for immediate surgery are (1) massive uncontrollable hemorrhage, (2) fulminating and diffuse toxic ulcerative colitis, with distention of the colon, (3) perforation with peritonitis, and (4) carcinoma arising in the course of the disease. Elective or probable indications for surgery are (1) unremitting diffuse disease of two or more years' duration, (2) repeated intestinal hemorrhage and persistent anemia or both, (3) diffuse, uncontrollable skin disease (pyodermas), (4) progressive deforming rheumatoid arthritis or spondylitis, (5) ocular disease (iritis, keratoconjunctivitis), and (6) uncontrolled disabling anorectal disease (fistulas, suppurative fissures, abscesses) leading to incontinence. In addition, certain surgical indications are contingent on progression of the disease, such as neurological manifestations like peripheral neuritis or cases of intractable disease in which the patient fails to maintain a satisfactory economic status.

The surgical treatment of ulcerative colitis has been greatly improved and simplified in the last decade. Surgeons now recognize that to effect a "cure" all of the diseased intestine must be removed and that morbidity is lowest for the one-stage colectomy as compared with the older multiple-stage procedures. The lower mortality of colectomy and simultaneous ileostomy in the critically ill patient and in the patient with toxemia, as compared with that of a diverting ileac stoma, is appreciated.

Colectomy is now performed through an incision in the left side of the abdomen, leaving the right side free for the ileostomy and the immediate application of soft, transparent, plastic bags for skin protection (fig. 1). Conventional ileostomy has largely been abandoned in favor of some form of eversion technique [1] with primary suture to the skin, which has resulted in normal small intestinal function within a few days after colectomy. This technique has eliminated the fluid and electrolyte problems and the nutritional failure previously observed during the postoperative period. The rapid return to health and vigor has made the ileostomy more acceptable to the patient, and the development of a variety of ingenious ileostomy appliances and skill in fitting them has done away with much of the danger of corroding the skin.

New Concept—Ileorectal Anastomosis

The practice of one-stage "removal of the disease" has led some surgeons to extirpate the colon and rectum at one operation. This eliminates forever the possibility of restoring intestinal continuity. In 1956, Aylett [2] reported his experiences with ileorectal anastomosis after colectomy. He pointed out that the success of the procedure depended on the removal of not only the colon but also the rectosigmoid. He further stated that after low ileorectal anastomosis the diseased rectal segment healed.

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Follow-up serial biopsy studies revealed mucosal surface healing, although restitution to integrity of the basic architecture of the submucosa could not be expected if it had been scarred by the disease. He presented clinical evidence to show that the lower part of the rectum would not only recover from active disease, but would function adequately as a terminus for the small intestine.

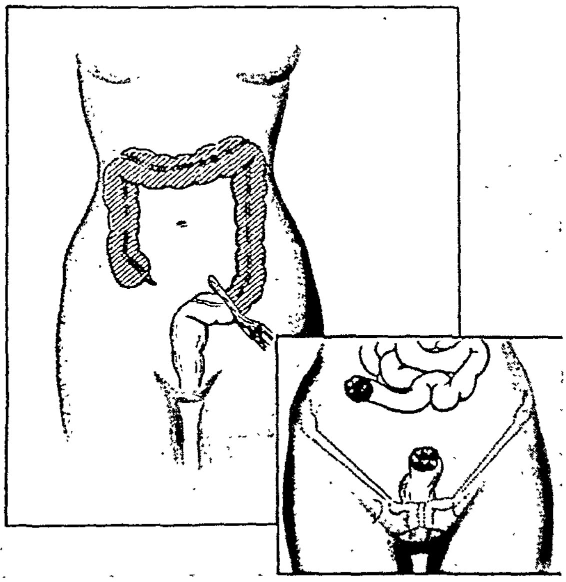

Fig. 1.—First stage of subtotal colectomy and ileostomy.

Aylett's interest in the possibility of ileorectal anastomosis was aroused by his clinical observation that the majority of patients with the diffuse form of the disease had minimal gross involvement of the ampulla of the rectum, while the area immediately above (rectosigmoid and sigmoid colon) was most ulcerated and deformed; e. g., pseudopolyps are often seen first at the rectosigmoid. He postulated that the rectum was least diseased because of its separate nerve supply and that it was kept inflamed by "drip-down" from the suppurative lesions above. Resection of the colon and the rectum down to a point below the deforming disease (about 4 in. above the anus) and mobilization of the lower part of the rectum from the presacral space not only would remove the gross deforming disease but would denervate most of the ampulla as well. Aylett[3a] has had excellent results in 100 patients with diffuse ulcerative colitis who have undergone colectomy with ileorectal anastomoses. His operative technique[3b] has been described in detail. He utilizes a two-stage procedure with a temporary ileostomy above the ileorectal anastomosis.

Since June, 1957, I have performed low ileorectal anastomoses in 14 patients having diffuse ulcerative colitis. The surgical technique differs from Aylett's in that (1) ileorectal anastomosis is done a year or more after subtotal colectomy and ileostomy, and (2) no decompressive ileostomy is done at the time of ileorectal anastomosis. The results so far have been satisfactory, although the number of patients is small and the observation period is short. More time and experience will be necessary for final evaluation, but it appears that the operation has a distinct place in the surgical treatment of this disease.

Technique.—Mobilization and resection of the rectum and sigmoid colon and low ileorectal anastomosis constitute the principal surgical maneuvers. Mobilization of the rectum involves the following procedures: The presacral space is entered medial to the left ureter and in front of Waldeyer's fascia. Sympathetic nerve trunks are preserved on either side. The peritoneal folds at the base of the mesorectum are incised part way down toward the rectovesical pouch or cul-de-sac, and the rectum is brought forward and upward from the sacrum by blunt dissection down to the tip of the coccyx. The middle hemorrhoidal vessels are not divided. The anterior peritoneal reflection is thus elevated to a comfortable position where the rectum may be cut across about 2 in. above it, and end-to-side anastomosis with the ileum is made (fig. 2). Important details in the technique are (1) dilatation of the open end of the divided rec-

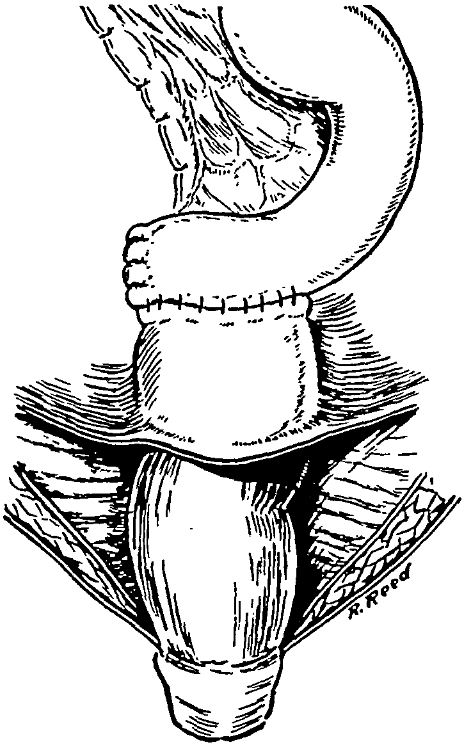

Fig. 2.—Second stage of resection of sigmoid colon and upper part of the rectum (ileoproctostomy).

tum if it is contracted; (2) for the anastomosis, the use of interrupted fine catgut sutures through all layers, and an outside seromuscular approximation with silk: interrupted sutures to avoid stenosis, and absorbable catgut to avoid through-and-through fistulas in the presence of active rectal disease; (3) the pelvis should not be reperitonealized, to allow accumulated blood to drain up into the abdominal cavity rather than to be confined at the anastomosis; and (4) the ovaries in premenopausal women should be sutured with silk to the round ligaments so that they will not prolapse into the presacral space where they may become extraperitonealized and cystic.

Early Results.—The primary disability after ileoproctostomy consists of multiple daily bowel movements which decrease within the first few weeks. The ileum above the anastomosis gradually dilates, as does the rectal ampulla. It is my opinion that more of the terminal ileum, if not diseased, could be saved at the time of colectomy, which would make possible a more solid bowel movement. Six of the patients in this series take antidiarrhea medication.

Aylett [3b] reports no recurrence of proctitis. We have not been so fortunate, although rectal disease present at the time of anastomosis has healed in all but three patients who had persistent disease of the rectum and suppurative cryptitis from three to six months after ileorectal anastomosis. Rectal continence has been well preserved except in the case of one patient who many years previously had sphincter damage and anal fistulas and now wears a pad for occasional leakage. Ileostomy has been reestablished for this reason. In all 14 patients incontinence of the rectum has occurred only for the first several movements after ileoproctostomy.

Sporadic reports of colectomy and ileoproctostomy have been published,[4] but from these accounts we cannot be sure at what level in the rectum the anastomosis has been made. This is most important, since according to Aylett [3] the retention of the involved pelvic colon or rectosigmoid is the principal cause of failure. To clarify this point, I would define the rectum as being 5 in. (15 cm.) in length above the dentate line. Ileorectal anastomosis is made below this level which, viewed within the abdomen at the time of surgery, would be 5 cm. or less above the peritoneal reflection (fig. 2). The lower level of resection would depend on the level of deforming disease, as it must be made below it.

With regard to the healing of the anastomosis between the diseased rectum and the normal ileum, although there was grossly recognizable ulcerative disease at the site of the rectal section all anastomoses performed on patients in this series have healed without formation of abscess or fistula. Care was taken not to spill intestinal contents, and each sigmoid colon was injected with a large volume of 1% neomycin sulfate solution prior to section and anastomosis. An indwelling rectal tube drained any accumulation of pus or stool during the mobilization period. Although the possibility of the development of cancer in the retained rectum must be conceded, I believe it is extremely unlikely since mucosal healing occurs after ileorectal anastomosis.

Failure of Ileoproctostomy.—Of 14 patients in whom ileoproctostomy was done there have been 4 who must be classed as clinical failures. In two the rectal disease has failed to heal. These patients are in moderately poor health and are disabled by frequent small bowel movements. The disease has not become worse nor is the adjacent ileum involved. Both refuse ileostomy. One other patient has already been mentioned as lacking sphincter control. Constant soiling of his perineum resulted in an uncontrolled dermatitis with pruritus, and he was relieved by reestablishment of the ileostomy. The fourth patient, a 15-year-old girl, had previously undergone subtotal colectomy and ileostomy. Much of the terminal ileum was found to be involved with ileitis; nevertheless, ileorectal anastomosis was done about a year later. Persistent ileitis has responded to medical management.

Conclusions

The indications for surgical treatment of ulcerative colitis are unchanged. The postoperative recovery period has been greatly shortened by the use of one-stage procedures and the construction of a physiological ileac stoma. Of the newer surgical concepts, the restoration of intestinal continuity by low ileorectal anastomosis is of particular interest. The results in the 14 cases herein reported indicate that there is a place for this procedure in the surgical treatment of this disease. With hope in sight for the avoidance of permanent ileostomy, the heretofore common practice of total proctocolectomy should be supplanted by subtotal colectomy, whenever the rectum and its sphincter mechanism have not been severely damaged by the disease.

2020 E. 93rd St. (6).

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ORGANIZATION AND OPERATION OF A POISON CONTROL CENTER

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To establish a poison control center means to create an agency that can communicate to a physician, under emergency conditions, the chemical composition of ingested substances and suggestions for diagnosis and treatment. The most important requisite for successful operation is a properly qualified professional person who, by reason of being compensated for his efforts, can devote a sufficient amount of time and energy to the program. Salaries therefore represent the largest items in the budget. Systematic use of the telephone as here described enables the center to function on a 24-hour basis, although at the Cleveland center 97% of the calls have come in between 8 a.m. and midnight. In addition to directly saving lives, the center has done much by means of education to prevent poisonings and serves as an excellent vehicle for improving public relations.

The statistics on accidental poisoning in the United States are grim. Probably close to a quarter of a million children under the age of 5 years ingest toxic or potentially toxic substances each year. Of these, about 300 to 400 will die. Two factors can reduce both of these figures—prevention and prompt, effective treatment. In recognition of this, the physicians of many communities have established poison control centers. It is probable that most communities will, in the near future, want to organize such a center to deal with their problems of accidental poisoning.

In the past five years physicians, and pediatricians in particular, have become acutely aware that accidental poisoning is an important, frequent, and serious problem. A major facet of this problem has been the fact that a great many household products sold to the American public do not give information on their ingredients, toxicity, or effective antidotes. This information is essential to the physician who has to treat cases of accidental poisoning involving these products. With more than a quarter of a million household items being sold and the number rapidly increasing each year, it is clear that the American youngster has potential exposure to substances that may lead to poisoning accidents.

We have, for the past two years, been concerned with the establishment and operation of a poison control center in a large metropolitan community. Previous to that we provided, over an eight-year period, information on poisoning to the medical community under a less formal and organized arrangement.

It appears desirable to record our experiences for several reasons, the most important being the fact that the fundamental principles underlying the establishment of a poison control center and its successful operation do not differ greatly whether the community is small or large. For the most economical use of energy and funds which become available for the establishment and maintenance of a poison control center, it is essential to know what has already been done and what is available and therefore need not be created *de novo* by each center.

Organization of a Poison Control Center

In June, 1957, the Academy of Medicine of Cleveland, with the aid of a grant from the Cleveland Foundation, started a poison control center. The establishment of a poison control center involves the creation of an agency or mechanism by virtue of which the physician, encountering a poisoning accident, can be "plugged-in" to the latest and most authoritative sources of information on the chemical composition of the ingested substances and on diagnosis and therapy.

There are now nearly 200 centers in the United States, and more are being formed. They do not all perform the same service. Some are information-dispensing agencies, others treat victims of poisoning accidents in addition, and a few have a still more complex organization and send trained personnel to follow up each accident with a home visit. Home visits produce data about the accidents which can be, and in some cases are, used to educate the rest of the community as to the nature of the hazard and possible steps that can be taken to avoid or minimize its recurrence.

The Cleveland center, in the first 15 months of its existence, has averaged 8-12 calls per day. Of these calls, 77% are from lay persons. Fifty-two per cent of the calls come between 8 a. m. and 4 p. m. and 3% between midnight and 8 a. m. Of the annual calls, 973 (31%) have involved medicaments, 603 (19%) household products, and 542 (17%) cleaning agents.

From the Poison Control Center, Cleveland Academy of Medicine.

The most important factor determining the successful operation of any poison control center is the acquisition of a properly qualified professional person or persons who can devote a sufficient amount of time and energy to ensure the proper functioning and continuity of the program. We feel that the only way to acquire this time in a reliable and continuing fashion is to pay for it. It is true, and undoubtedly will remain true, that some communities will be blessed with interested persons who will devote the requisite amount of time, for a short period, without remuneration. However, it is our belief that the great majority of communities wishing to establish a poison control center, however small, will not be so fortunate. We would recommend that the primary use of money available for the establishment of a center should be the remuneration of a professional person who will regularly and continuingly devote a definite amount of time to the direction of the center. In the Cleveland experiment, one of the first steps was to secure the services of a medical director and a technical director. Their salaries, and that of a part-time secretary, represent the largest items in the financial aid requested and received for this project.

Duties of a Director.—In small communities, the director may be the embodiment of the center—he will take all calls, will be the repository for the stores of information available, and, perhaps, will act as a consultant in cases of poisoning. In most instances, however, he can be far more effective if his time is spent in organizing and controlling the various facilities needed to operate the center, assembling sources of information, and keeping them up to date. In addition, the director can initiate and supervise programs designed to educate physicians in the proper management of poisoning cases and to acquaint lay persons with the hazards and prevention of accidental poisoning and with the proper utilization of facilities available for the treatment of such cases. The following description of these duties is based on the program at the Cleveland center.

The technical director, a chemist and toxicologist, was appointed to organize material on the vast number of chemical substances included in the formulations of products involved in poisoning. Under his direction, a comprehensive library of books and pamphlets was assembled and kept up to date to provide specific as well as general information about the chemical composition of individual products as information was obtained from many different sources. Community resources were utilized to obtain consultants in various specialty fields, such as botanicals, economic poisons, protective coatings, and industrial chemicals. All these persons are on 24-hour call. If local resources are inadequate, the telephone brings any area of the United States within relatively easy reach for prompt resolution of a special problem.

A medical director, an internist, was appointed to deal with the problems of therapy and with clinical aspects of poisoning. In addition, a group of physicians with highly specialized interests is available for consultation.

Facilities.—Poisoning accidents are emergencies which may arise at any time and which require immediate attention. At this center, dialing a well-advertised telephone number connects the caller with the operator at the Academy of Medicine's 24-hour call service. This operator will, through a direct line to the University Hospitals, contact the resident physician on call for poisoning cases. At this hospital, members of the senior resident staff of the pediatrics service rotate through the duties of poison control officer as an integral part of their training. In every case the operator gets the name, telephone number, and agent involved and ascertains whether the patient's private physician has been called. This information is taken while the operator is awaiting the poison control officer's answer. Every effort is made to have the patient contact his private physician, and his call is put through to the poison control officer only when the private physician cannot be located or in cases in which urgency is apparent or in cases in which the caller has no private physician. An advantage of routing all calls through the Academy of Medicine telephone service is that these operators are skilled in locating physicians and can be doing this while the patient is speaking with the poison control officer or is on his way to a hospital emergency room.

The sole function of the poison control officer is that of supplying information. To this end, a complete library of books, pamphlets, and memorandums on poisoning is kept in one or more strategic locations in the hospital. A list of these books has been published.[1] At the Cleveland center, the poison control officer has other hospital duties which keep him in the vicinity of a telephone in an outpatient department office during the day. This telephone is a special line, used only for calls on poisoning, so that there will be no hold-up due to busy hospital lines. The major, and most complete, library of information is kept in this outpatient department office, since the vast majority of calls come during the day. After 4 p. m. the poison control officer is either at Babies and Childrens Hospital, where he can readily use the main library, or else he is in the hospital emergency room or in his living quarters. Duplicates of the most useful sources of information have been placed in each of the latter two places. If the poison control officer is not near the special telephone, the Academy of Medicine's call service operator can call the University Hospitals on a private trunk line that eliminates delays. From the hospital, where a Telepage call system is used, the poison control officer is called as "Doctor Pico" (abbreviation for poison information center officer). By using this system, the operator need not know the name of the current poison control officer. Furthermore, should the latter not respond to his call other physicians will call in and take over.

Cuyahoga County covers a large metropolitan area of northeastern Ohio. Physically it was not practical and professionally it was undesirable to have one center in this area. However, the problem of prompt, effective treatment of poisoning accidents is a real one. Recognizing this need, the Academy of Medicine center urged the respective staffs of the local hospitals to create treatment centers at their hospitals. These treatment centers are under the supervision of a visiting physician and are primarily designed for therapeutic activities. Nineteen local hospitals instituted this program, generally under the aegis of a pediatrician. Periodic meetings have been held by this group and the professional staff of the center to discuss mutual problems and recent advances. A protocol for treating a poisoning emergency was drawn up by this group and made an integral part of the respective hospital's procedure. A poison therapy cart has also been described.[1] At a recent meeting it was suggested that another visiting physician be added to the treatment center's staff at each hospital so that an internist and a pediatrician would be available for consultation. Each visiting physician, in addition to consulting with the resident staff on specific problems as they occur, arranges periodic staff meetings to discuss the many problems attendant on proper and effective therapy for victims of accidental poisoning. These meetings generally center about a recent particular local poisoning case and serve to educate the house and visiting staff.

Consultants and Special Facilities.—The efficacy of the poison control center can be significantly increased by use of the technical resources of the community it serves. Thus, it would be well to know the nearest location of an artificial kidney and of a laboratory wherein chemical analyses of body fluids can be done on an emergency basis. In the industries, schools, museums, and health departments of a community, persons can be found who will willingly serve, on a 24-hour basis, as helpful consultants on the identification of botanicals, paints, cleaners, medicaments, and industrial and agricultural chemicals. Such a group of consultants has been invaluable in the operation of this center.

Educational Activities

The circumstances surrounding poisoning accidents are strikingly similar and are such as to convince one that a program designed to educate those who supervise the activities of children under 5 years of age would return a handsome dividend in lives saved and illness prevented. Such a program involves the continuing and repetitive education of medical people, such as physicians and nurses, as well as of nonmedical persons, such as parents, baby sitters, firemen, and policemen. The outline of the educational program sponsored by the Cleveland center, given below, is a guide to what can be done. It should be apparent that this venture consumes time, money, and energy and may well be beyond the immediate objective possible for any such poison control center unless cooperative and collaborative efforts can supply the center with educational material so essential for an educational program.

Education of Physicians.—The following items are included in the educational program for medical people: 1. Lectures, conferences, and clinical-pathological exercises are designed to bring out the problem of poisoning, its diagnosis, its pathological physiology, and its therapy. 2. Articles on poisoning, published in a journal having wide circulation among the local practitioners, are used. The Cleveland center has published articles on the general aspects of poisoning and its therapy and on specific poisonings (salicylate, lead) in *The Bulletin of the Cleveland Academy of Medicine.* The National Clearinghouse for Poison Control Centers puts out an excellent monthly bulletin on the various aspects of poisoning which is distributed to local physicians in charge of treatment centers. 3. Meetings between the professional staff of the center and the physicians representing the local hospitals provide a great deal of mutual education in the way of new therapies, pertinent publications, and interesting cases encountered. 4. Reprints and abstracts of pertinent articles are prepared at the center and distributed to the participating hospitals and, through the latter, to any interested physician. 5. Some pharmaceutical firms publish excellent brochures on the various aspects of poisoning; these are obtained by the center and distributed locally.

Education of Nonmedical People.—Education of nonmedical people involves the following procedures: 1. The physician has an important role in educating the public to the prevention and proper treatment of poisoning. He can place literature in his waiting room. He has the unparalleled opportunity repetitively to bring up the topic of prevention of poisoning accidents to patients who care for small children. When prescribing medicaments, he can stress proper safeguarding and disposal when the drug is no longer needed. By being willing to lecture on this topic to the Parent-Teachers Association and similar groups, he can reach a much larger audience. 2. Pamphlets can be distributed through physicians' offices, pharmacies, visiting nurses, and well-child clinics. A folded, 8-by-11-in., red, black, and white pamphlet on the danger of household preparations was designed at this center. Its theme was "out of sight, out of reach helps keep your child out of trouble." More than 100,000 of these pamphlets have been requested in the past two months. 3. The Cleveland center helped organize and sponsor a poster contest for school children, in cooperation with the Cleveland Board of Education and the Catholic Board of Education. The

Causes of Death in Immature Infants.—The principal cause of death in immature infants was premature rupture of the membranes. Premature rupture of membranes has generally not been listed as an important item in perinatal mortality. A recent study in the three teaching institutions in North Carolina indicated that 15.8% of all deliveries were complicated by this condition while 26.7% of all perinatal deaths were associated with premature rupture of membranes.[4] Believing this complication to be of significance, preference was given to it when there were no other obvious causes of death. Toxemia of pregnancy was an important factor in the deaths of 15.4% of these small infants. Premature separation of the placenta as well as rupture of the marginal sinus accounted for 12.8% of the deaths. Birth injuries, generally associated with anoxia, accounted for 7.7% of these deaths in immature infants.

Socioeconomic Aspects

Recent studies have indicated the importance of parental, fetal, and environmental factors in perinatal mortality.[5] These same factors were found to be important in this material.

Table 3 shows the perinatal mortality in the North Carolina Memorial Hospital according to race and admission status. The perinatal mortality of all deliveries was 48.8 per 1,000 births; for premature and mature infants it was 34.5. When one compares the mortality among the staff patients with that in private patients and similarly for nonwhite and white patients, it is evident that the majority of the deaths were among staff and nonwhite infants. This is even more apparent when the perinatal mortality for the nonregistered group is reviewed. The nonregistered patients were generally indigent white and nonwhite mothers referred from rural hospitals and clinics. The mortality of these immature unregistered infants was 294.9 per 1,000 births, while the death rate for the premature and mature infants was 160.3. When the unregistered group is eliminated from the data, the perinatal mortality in the registered staff and private group approaches a reasonable and acceptable rate of 27.2 and 23.3, respectively, per 1,000 births.

TABLE 3.—*Perinatal Mortality at North Carolina Memorial Hospital According to Race and Admission Status*

Status	Deliveries, No.	Perinatal Mortality per 1,000 Births: 400 Gm. and Above (Total)	Perinatal Mortality per 1,000 Births: 1,000 Gm. and Above
All deliveries	2,728	48.75	34.45
Staff deliveries	1,737	61.02	39.14
Private deliveries	991	27.24	26.23
White	1,816	33.31	27.53
Nonwhite	912	77.85	48.24
Nonregistered*	156	294.87	160.25
Staff-registered	1,581	37.95	27.19
Private-registered	987	23.27	23.27
Total registered	2,568	32.32	25.70
Total	2,728	48.75	34.45

* No prenatal care at North Carolina Memorial Hospital.

There is a striking contrast between the causes of death in private patients and unregistered patients. Malformations accounted for 25.9% of the infant deaths among private patients, while there were no deaths from this cause among nonregistered patients. Toxemia of pregnancy was the principal cause of death in 7.4% of the private patients but 37.5% and 27.3% of the nonregistered group. Premature rupture of membranes did not contribute to a single death in the private patient group, but it was a major factor in the death of 8.3% of the premature and mature infants and 27.3% of the immature infants among nonregistered patients. When major obstetric complications do not occur in a group of patients, there will be an increase in the percentage of nonpreventable causes of death, such as congenital malformations and erythroblastosis.

TABLE 4.—*Cause of Death Among Private and Unregistered* Patients Delivered at North Carolina Memorial Hospital, 1952-1958*

Cause of Death	All Private Patients No.	All Private Patients %	Unregistered Patients: 1,000 Gm. and Above No.	Unregistered Patients: 1,000 Gm. and Above %	Unregistered Patients: Under 1,000 Gm. No.	Unregistered Patients: Under 1,000 Gm. %
Placenta previa	3	11.1	0	0	0	0
Premature separation of placenta or marginal sinus rupture	4	14.8	4	16.7	2	9.1
Prolapse or compression of umbilical cord	1	3.7	0	0	1	4.5
Maternal complications	1†	3.7	2	8.3	1	4.5
Complications of labor	0	0	1	4.2	0	0
No abnormal state	4	14.8	1	4.2	0	0
Toxemia of pregnancy	2	7.4	9	37.5	6	27.3
Diabetes mellitus	1	3.7	3	12.5	0	0
Birth injury	1	3.7	0	0	1	4.5
Malformations	7	25.9	0	0	0	0
Erythroblastosis or ABO incompatibility	3	11.1	0	0	0	0
Infection	0	0	2	8.3	1	4.5
Premature rupture of membranes	0	0	2	8.3	6	27.3
Abnormal pulmonary ventilation	0	0	0	0	4	18.2
Total	27	100.0	24	100.0	22	100.0

* No prenatal care at North Carolina Memorial Hospital.
† Poliomyelitis.

Table 4 compares causes of death in the private and unregistered groups. *Perinatal mortality due to* premature rupture of membranes is clearly a complication among nonwhite staff patients; it was associated with 25.6% of the perinatal deaths. When premature rupture of membranes occurs among infants weighing over 2,000 Gm. (4½ lb.) in the white private patients, it is of minor importance; but when this complication occurs in lower socioeconomic groups, both white and nonwhite, it is a particularly lethal complication.[4]

Table 5 shows data on toxemia of pregnancy and premature separation of the placenta and rupture of the marginal sinus in regard to status of the patient. Toxemia of pregnancy is also seen to be a complication among nonwhite staff patients. Thirty per cent of all deliveries on the obstetric service are nonwhite, but 70% of the cases of toxemia of pregnancy occurred in this group. Moreover, 93.3% of the cases of toxemia occurred among staff patients, but only 6.7% of the cases occurred among private patients. It is important to note that 22.6% of all of the infant deaths were associated with toxemia of pregnancy.

Premature separation of the placenta and rupture of the marginal sinus also were related to the socioeconomic status of patients. Of the total of these hemorrhagic complications, 55.6% occurred in nonwhite mothers, while only 30% of the deliveries were in this group. Of the total cases of premature separation of the placenta or marginal sinus rupture, 77.8% occurred in staff patients, while 22.2% occurred in private patients. Of all the perinatal deaths, 13.5% were associated with this complication.

TABLE 5.—*Analysis of Premature Rupture of Membranes and Toxemia of Pregnancy as Causes of Perinatal Deaths*

	Premature Rupture of Membranes*		Toxemia of Pregnancy†	
	No.	%	No.	%
Race and admission status				
Nonwhite	22	64.7	21	70.0
White	12	35.3	9	30.0
Staff	31	91.2	28	93.3
Private	3	8.8	2	6.7
Registered	26	76.5	11	36.7
Unregistered	8	23.5	19	63.3
Birth weights, Gm.				
400 to 999	16	47.2	6	20.0
1,000 to 2,499	13	38.2	14	46.7
2,500 and above	7	20.6	10	33.3
Importance as cause of death				
Primary	20	58.8	20	66.7
Contributing	8	23.5	5	16.7
Miscellaneous factors				
Associated with premature separation of placenta	5	14.7	3	10.0
Febrile (above 99 F)	12	35.3	7‡	23.3‡
Not febrile	22	64.7	..	...

* 25.6% of all with premature rupture of membranes.
† 22.6% of all deaths were associated with toxemia of pregnancy.
‡ Associated with fetal distress.

A previous review [5a] of the material in the North Carolina perinatal mortality study revealed that the father's occupation and the mother's education were probably of major importance in fetal and neonatal deaths. The death rates per 1,000 single births of infants weighing 400 Gm. and above, according to three occupation groups of the fathers, are as follows: group 1 (professional people, managers, officials, proprietors, and university students), 29.5 for white infants; group 2 (clerks, sales workers, craftsmen, foremen, and operators), 53.6 for white infants and 46.2 for nonwhite; and group 3 (farmers, farm laborers, other laborers, and household workers), 111.8 for white infants and 82.2 for nonwhite. It is clearly evident that the father's occupation is significant in its relationship to perinatal mortality. Figures for white and nonwhite persons should not be compared, since the occupations of many of the nonwhite fathers were not known and therefore could not be used in the tabulations.

The perinatal deaths, per 1,000 births, in relation to the education of the mother are as follows: among those with more than 12 years of education, 28.0 for white infants; 9-12 years, 65.7 for white infants and 48.9 for nonwhite; and 8 years or less, 70.5 for nonwhite infants. There were insufficient cases for an analysis of nonwhite mothers with more than 12 years of education and white mothers with 8 or less years, but the data available show a distinct correlation with the mother's education and perinatal mortality.

Incidence of Cesarean Section

Eastman [6] has indicated that the incidence of cesarean section in maternity hospitals is between 2 and 6%. There are, however, some private hospitals with a cesarean section rate of over 10%.

The incidence of cesarean section in the North Carolina Memorial Hospital for the five-year period, for a total of 2,700 deliveries, was 58, or 2.15%. However, the incidence among 1,717 staff patients was 27, or 1.57%, and the rate for 983 private patients was 31, or 3.15%. A review of each perinatal death indicated that a more conservative attitude was taken concerning cesarean sections among staff patients than among private patients. There were nine possibly indicated but not performed sections among staff patients but only one section which was possibly indicated but not performed among private patients. Had these 10 patients had abdominal deliveries, the incidence of cesarean section for the service would have been 2.52% and the incidence among staff and private patients would have been 2.09% and 3.25% respectively.

The section rate among staff and private patients should be about equal, with the incidence of the operation being slightly higher among staff patients. It is important to audit at periodic intervals the cesarean sections done on a service so that the incidence of the operation among private patients does not become too high while the incidence of the operation among staff patients does not remain too low.

Possible Errors in Obstetric Management

It is sometimes difficult but always important to analyze all perinatal deaths for possible errors in obstetric and pediatric management. There were 133 perinatal deaths among the 2,728 deliveries between 1952 and 1958. There were 12 deaths (9%) where the obstetric management of the patients while they were in the North Carolina Memorial Hospital possibly could have been improved.

Fetal Distress.—There were five cases of error in the management of fetal distress. Cesarean section probably should have been performed in four of these. Induction was not done in the case of a postmature infant with premature rupture of membranes and the passage of meconium. Concealed hemorrhage was not promptly diagnosed and treated. There was a delay in the diagnosis and treatment of a patient with prolapse of the umbilical cord. Oxytocin (Pitocin) stimulation was continued despite a persistent bradycardia (100 to 110 per minute) in a patient with severe toxemia of pregnancy. Another patient was not properly observed during oxytocin stimulation.

Toxemia of Pregnancy.—The principal errors in the management of patients with toxemia of pregnancy were due to the failure to realize the importance of albuminuria and a reduction in fetal growth. One patient, with severe toxemia, had fetal death in utero when there was an inordinate delay in induction. A second patient had persistent albuminuria and failure of the uterus to increase in size over a four-week period. Fetal death in utero occurred before induction was attempted. A third patient was not promptly admitted to the hospital when severe toxemia developed.

Diabetes.—The major causes of perinatal deaths in pregnant diabetic women in the North Carolina Memorial Hospital has been a failure of referring physicians to provide proper prenatal care and a failure of the patients to cooperate in the obstetric and medical management of their diabetes. There was no correlation between the perinatal mortality among pregnant diabetic women in this hospital and White's classification of such patients[7]; the death rates were a function of the intelligence and socioeconomic status of the mother. Cesarean sections, however, should probably have been done on two patients with excessively large infants, one patient with an abnormal presentation, and one patient with uterine inertia.

Anesthesia and Analgesia.—It is difficult to assess the role of anesthesia and analgesia in perinatal mortality because of the multiplicity of factors that are so often present in an infant's death. However, each death was carefully reviewed as regards to the role played by anesthetic and analgesic agents. It was felt that there were no deaths in mature infants which were related to analgesic or anesthetic drugs. In 25 of the 45 premature infants who died in the neonatal period, however, mothers received at least one analgesic or anesthetic agent during labor. It is felt that this is not consistent with the best obstetric practice. In general, premature infants have the best chance of survival when no analgesia or anesthesia is used and delivery is conducted with the patient under a pudendal block and with administration of 100% oxygen.

Neonatal Deaths

The autopsy material and clinical records of the 63 neonatal deaths were reviewed in order to determine the causes of death of these infants. The major problems of the neonatal period were prematurity in 26 cases, birth injury in 13, and infection in 9. These and other factors in neonatal deaths are summarized in table 6.

Summary and Conclusions

A study of the perinatal mortality in 2,728 deliveries conducted in the North Carolina Memorial Hospital showed the principal causes of death to be hemorrhagic complications, toxemia of pregnancy, congenital malformations, and premature rupture of the membranes. It is felt that premature rupture of the membranes should receive increased attention as an important cause of perinatal mortality. There was a significant correlation between the socioeconomic status of the patients and perinatal mortality. The highest perinatal mortality occurred among the lower socioeconomic group of patients, whether the classification was based on the mother's education, on race, or on the father's occupation.

TABLE 6.—*Autopsy Findings or Clinical Diagnoses in Sixty-three Cases of Neonatal Deaths at North Carolina Memorial Hospital, 1952-1958*

	Total
Prematurity	26(41.1%)
Alone	9
With atelectasis	15
With ventricular hemorrhage	1
With adrenal hemorrhage	1
Postnatal asphyxia and atelectasis	3(4.8%)
Atelectasis alone	1
Hyaline membrane	2
Infection	9(14.3%)
Pneumonia with maternal sepsis	3
Pneumonia, cause unknown	2
Septicemia with maternal sepsis	1
Meningitis with traumatic delivery	1
Enterocolitis and pneumonia	1
Sudden death with tracheitis	1
Congenital malformations	8(12.7%)
Multiple, severe	2
Congenital diaphragmatic hernia	2
Polycystic liver and kidneys	1
Nephroblastoma and polydactyly	1
Esophageal atresia	1
Ileal atresia	1
Birth injury	13(20.7%)
Subarachnoid or subdural hemorrhage*	12
Traumatic delivery	1
Erythroblastosis	2(3.2%)
Fetal hydrops	1
Severe early jaundice and kernicterus	1
Sudden death with no significant findings	1(1.6%)
Unknown	1(1.6%)

* 11 in premature infants.

The principal errors in obstetric practice were related to the management of fetal distress, toxemia of pregnancy, and diabetes. A reduction in perinatal mortality can occur with improved obstetric care. This reduction will be most significant when it is associated with an improvement in the socioeconomic status of the obstetric patients and a reduction in the birth rate among indigent mothers.

North Carolina Memorial Hospital.

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UROLOGIC PROBLEMS IN REHABILITATION OF HEMIPLEGIC PATIENTS

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The records of 254 patients with hemiplegia resulting from cerebral vascular accidents have been studied for evidence of an association between urinary incontinence and ability to regain ambulatory status. The patient who has had a stroke must be watched for evidence of urinary dysfunction, especially since incontinence may be evidence of retention. Its persistence is not always due to impairment of cortical control; it may be the result of coincident urologic disease. The data from this study showed that persistent urinary incontinence was associated with delay or failure of the recovery process with respect to ambulation, but the causal relation was complicated. The functions of ambulation and urination are both impaired by the loss of cortical control, but incontinence also causes difficulties in transportation and in rehabilitative procedures. The control of incontinence by the various measures suggested here is an important step in the rehabilitative process.

In a previous investigation[1] into the causes for failure to achieve independent ambulation in a group of hemiplegic patients, we noted that a high proportion of the patients with failures had associated urinary incontinence. Our purpose, therefore, has been to see if incontinence played a significant role as a cause for failure to achieve independent ambulation and to study the relationship of incontinence to other factors which are present, such as the mental status, emotional status, positive motivation for independence, severity of the muscular involvement, and aphasia. We were interested in the effects of the central nervous system lesions as well as in the possibility of local pathology within the genitourinary tract as further complicating problems. Some of these local pathological problems were preexistent to the hemiplegia, and others developed as complications of the stroke. In the past, it has been generally felt that persistence of incontinence is a poor prognostic sign for independence. We were interested in seeing if this were true on the basis of our own cases and in determining if there

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were other correlations which might be of value in prognosis as to recovery of bladder control and achievement of independent ambulation.

Method

We have reviewed the records of 254 consecutive inpatients admitted to the rehabilitation service of the Burke Foundation with the diagnosis of cerebral vascular accident resulting in hemiplegia. Patients were unselected and were not screened prior to admission. The cases were previously classified at time of discharge only in terms of ambulation as (1) success (completely independent with or without cane or brace), (2) premature discharge (insufficient time for recovery or therapy), (3) unfeasible for rehabilitation (general medical or mental condition unsatisfactory), (4) deteriorated (became acutely ill and therapy discontinued), or (5) failure. The failures, in terms of completely independent ambulation, were classified as "true failures" (TF) if ambulation was safely limited to parallel bars even with maximum support by a therapist, "assistance" (A) if patient required minimal assistance to give support or balance outside of parallel bars, or "observation" (OBS) if patient required observation outside the parallel bars to provide occasional assistance for balance and support. Patients in groups A and OBS generally could be expected to walk satisfactorily about the ward or home with an attendant or relative and thus are failures only in the sense of our definition of terms, the condition actually having improved significantly. Many in groups A and OBS also would be expected to continue to improve after discharge and ultimately arrive in our success group.

All patients who manifested urologic problems were analyzed as to success and failure in ambulation, diagnosis of urologic problems, age, sex, presence or absence of organic mental syndrome, emotional state, site of lesion, bilateral or multiple involvement, associated illness, recovery of urologic problems, and aphasia.

Physiology of Micturition

The bladder is controlled by two reflex mechanisms: 1. The spinal (cord) mechanism consists of an afferent and efferent limb synapsing in the sacral cord. Filling of the bladder is an adequate stimulus for this arc. When a sufficient threshold is reached the motor impulse is carried over the efferent limb resulting in contraction of the bladder detrusor urinae. 2. The suprasegmental (cortex, midbrain, and hindbrain) mechanism consists of afferent and efferent pathways between the brain and the cord. The afferent pathways carry the impulses of bladder sensation to consciousness, while the efferent pathways carry tonically active subconscious inhibitory impulses which prevent involuntary contraction of the bladder in adults and maintain sphincter tone.

Micturition results from a stretch reflex (spinal reflex) or the reaction by contraction of muscle fibers to the stimulus of stretching. The reflex center is in the sacral portion of the spinal cord. Impulses from the distending bladder wall constantly reach the reflex center, but stimulation of the efferent (motor) parasympathetic neurons to cause detrusor contraction is inhibited by impulses from centers in the brain or brain stem. This activity remains below the level of consciousness until vesical distention or intravesical pressure reaches a critical level, at which point the individual becomes aware of a desire to void. If the time and place are not propitious, inhibiting impulses may be sent voluntarily down to the sacral cord to postpone micturition. When desired, these impulses are suppressed and the detrusor muscle allowed to contract in response to the stretch reflex. Voiding is facilitated by contraction of the abdominal muscles and lowering of the diaphragm. The vesical neck gradually opens, the external sphincter opens abruptly, and voiding takes place. Contraction of the detrusor muscle is maintained until all of the urine is evacuated, and this is believed to be a manifestation of cerebral control.

TABLE 1.—*Types of Urologic Problems in Hemiplegic Patients During Rehabilitation*

Group	Patients, No.		Condition	Manifestation
	Men	Women		
Ambulatory	4	5	Loss of cortical inhibition	Incontinence of bowel and bladder
	3	1	Loss of cortical inhibition	Nocturnal incontinence
	1	...	Benign prostatic hypertrophy-prostatitis	Hematuria
	...	3	Cicatricial urethritis	Retention and incontinence
Nonambulatory	19	18	Loss of cortical inhibition	Incontinence of bowel and bladder
	1	...	Loss of cortical inhibition and postoperative carcinoma of prostate	Incontinence of bowel and bladder
	...	6	Loss of cortical inhibition and cicatricial urethritis	Incontinence of bowel and bladder and retention
	3	2	Loss of cortical inhibition	Nocturnal incontinence
	3	1	Loss of cortical inhibition	Urinary incontinence
	2	...	Benign prostatic hypertrophy	Frequency
	2	...	Vesical neck obstruction with benign prostatic hypertrophy	Slight retention and frequency
	1	...	Vesical neck obstruction with benign prostatic hypertrophy	Complete retention
	...	1	Postoperative retention	Frequency; dysuria
	...	7	Cicatricial urethritis	Retention and incontinence

Results

In our group of 254 hemiplegic patients, 138 achieved independent ambulation prior to discharge. This is the success group. One hundred sixteen patients did not achieve independent ambulation; 64 of these were in the failure group, due to the neuromuscular status, and 52 were considered to be in the unfeasible, deteriorated, or premature discharge groups. Of the total group of hemiplegic patients, 83 (32%) (table 1) were found to have had urologic problems during their period of rehabilitation. Of these, 17 were in the success group and 66 in the failure and unfeasible group.

The 17 patients in the success group who had urinary problems included 13 with lack of cortical inhibition, manifested in 9 by incontinence of bowel and bladder and in 4 by incontinence of bladder at night. This group consisted of 6 females and 7 males, and at the time of discharge 10 had become continent, 1 had improved, and only 2 remained incontinent of urine at night. The sex distribution of patients does not appear to be significant. There were 13 instances, however, of patients who manifested various degrees of organic mental syndrome and 8 instances of emotional disturbances which tended to clear up with improvement in control. Multiple strokes occurred in only one patient. Vesical neck obstruction occurred in three female patients in whom a diagnosis of cicatricial urethritis had been made. Manifestations included urinary retention, frequency, urgency, and incontinence, chiefly nocturnal. Two of these patients became continent and symptom free, and one improved after treatment. Benign prostatic hypertrophy occurred in one male patient and was manifested by gross hematuria which cleared spontaneously after a period of catheterization with an indwelling catheter. In neither the vesical neck obstruction cases or the benign prostatic hypertrophy case was an organic mental syndrome present.

TABLE 2.—*Characteristics of Continent and Incontinent Patients*

Group	Total	Hemiplegia		Organic Mental Syndrome	Emotional Disturbance	Bilateral Involvement	Multiple Involvement	Aphasia
		Right-Sided	Left-Sided					
Continent, successful rehabilitation								
Male	76	38	38	10	41	3	6	31
Female ..	45	17	28	3	22	2	6	14
Continent, unsuccessful rehabilitation								
Male	23	9	14	5	14	1	4	6
Female ..	27	12	15	5	16	2	3	9
Incontinent, successful rehabilitation								
Male	8	2	6	6	3	..	..	1
Female ..	9	5	4	7	5	..	1	2
Incontinent, unsuccessful rehabilitation								
Male	31	13	18	26	13	6	6	11
Female ..	35	18	17	27	15	5	5	17

The 66 patients in the failure group who had urinary problems included 52 with loss of cortical inhibition due to the cerebral vascular accident; this was manifested in 37 by incontinence of bowel and bladder, 4 by urinary incontinence—day and night, 5 by nocturnal urinary incontinence, and 6 by incontinence of bowel and bladder complicated by cicatricial urethritis.

Fourteen patients manifested primary urologic problems; seven females had frequency, urgency incontinence, and dysuria secondary to cicatricial urethritis, with retention of urine and cystitis. All of these patients became continent. Five males had retention with urgency incontinence and nocturnal incontinence with secondary retention and cystitis due to benign prostatic hypertrophy. One male initially showed bowel and bladder incontinence secondary to loss of cortical inhibition, but as this cleared he manifested a premorbid urinary incontinence which had been present after a prostatectomy for carcinoma with apparent sphincter injury. One female patient, who had undergone hamstring release, developed urinary retention postoperatively due to poor bladder emptying and developed a cystitis with urgency incontinence. After treatment she became continent.

There is no significant difference in the characteristics of incontinent males as compared to incontinent females in either the success or failure groups, with the exception that the males were slightly older. Males and females showed essentially the same incidence of right-sided and left-sided hemiplegia, aphasia, incidence of bilateral or multiple involvement, incidence of cardiovascular disease, emotional disturbances, and organic mental syndromes. There is no significant difference between the sexes in incidence of urologic problems in either the success or failure groups (table 2).

When we compare the success group with the failure group of incontinent persons, regardless of sex, there is no significant difference of incidence of right-sided and left-sided hemiplegia, organic mental deficits, or emotional disturbance, but there is an increased incidence of aphasia, second strokes, and bilateral involvement in the failure group as compared to the success group. It is felt the organic mental changes were more severe in the failures.

The outstanding fact noted is the much greater incidence of urologic problems in the failure group—66 cases out of 116, or 56%, as compared to 12% of the success group. This failure group is made up of those patients for whom rehabilitation is considered unfeasible and those patients who did not achieve independent ambulation by the time of discharge. Among the incontinent failures were 22 cases of multiple strokes or bilateral involvement. In the failure group of 31 patients with hemiplegia on the right, 28 had aphasia; in the successful group 3 cases of aphasia occurred in 7 patients. Thus, there was a higher incidence of aphasia in the failure group. Of the 67 incontinent failures, 53 showed organic mental changes, as did 13 of the 17 in the successful group. The primary cause was loss of cortical inhibition alone in 56 patients, with cicatricial urethritis in six and benign prostatic hypertrophy in one. Seven patients had cicatricial urethritis alone, and six had benign prostatic hypertrophy alone.

The continent patients, as compared to the incontinent, showed a majority of successes and a decreased incidence of organic mental changes, multiple strokes, and bilateral involvement. Aphasia in all groups occurred in a majority of patients with hemiplegia on the right; it did not appear to be significantly higher among the incontinent patients as such but was slightly higher in the failure group of both the continent and incontinent patients.

Observations After Cerebral Vascular Accident

During the initial phase of a stroke, with or without loss of consciousness, as a result of the neurological lesion, there is an interruption in the normal pathway of afferent impulses from the bladder wall to the cerebrum and the efferent pathways which permit cortical inhibition of the reflex of micturition. The loss of cerebral inhibition over reflex bladder contractions results in frequency, urgency, and urgency incontinence (precipitate micturition), not unlike that in a patient with uninhibited neurogenic bladder.

Bilateral lesions of the motor cortex usually give rise to such characteristic disturbances as (*a*) inability to initiate micturition voluntarily, (*b*) inability to stop the stream, and (*c*) urgency, frequency, and urgency incontinence due to lack of cerebral inhibition. The bladder is overactive and hyperirritable. The external sphincter may become hypertonic or even spastic with resultant retention.[2] The more extensive the lesion the more likely that bilateral dysfunction may occur, at least temporarily, and thus the greater likelihood of impaired cortical inhibition.

Thus, to a certain limited extent the situation is similar to that which occurs in a spinal cord transection with the development of an automatic bladder. In hemiplegia, of course, the situation is not as marked and generally there is recovery, since only the tracts of one side of the brain are affected and usually only temporarily. The loss of cortical inhibition of micturition permits the detrusor to contract frequently and with little force, thus giving rise to incontinence with urination occurring frequently in small amounts day and night. Normally, as the bladder fills and distends, cortical inhibition prevents urination through the action of the external sphincter and through inhibition of these mild detrusor contractions. Secondarily, in this phase, there is also a tendency for the bladder not to empty completely, so that there is usually some degree of residual urine. At times, urinary retention may be marked, particularly if some form of obstruction of the vesical neck is already present, and acute urinary retention may occur.

Prostatism in men is frequent in the stroke age group and contributes to retention, as does chronic cicatricial urethritis in the female. Retention may occur while the patient is unconscious, but with return of consciousness continued marked retention is uncommon, except in those with associated obstruction. After the acute phase of the cerebral vascular accident catheterization or an indwelling catheter may be necessary for prevention of the incontinence due to the loss of cortical inhibition, or it may be necessary also to prevent urinary retention due to this condition, plus a premorbid tendency to vesical neck obstruction which increases the amount of urinary retention.

Normally, as the patient regains consciousness and improves, cortical inhibition returns and the patient will regain normal bladder function. In a certain number of patients with hemiplegia, however, urinary incontinence continues as a problem. This is due to several factors, as follows:

1. The neurological impairment of the pathways may be such as to prevent normal function of cortical inhibition.
2. Organic mental changes with clouding of the sensorium or loss of motivation for control may cause the patient not to respond to the sensory stimuli of bladder distention and permit reflex emptying without cortical inhibition.
3. Preexisting vesical neck obstruction (such as prostatic hypertrophy in the male and cicatricial urethritis in the female) may have caused symptoms prior to the cerebral vascular accident. In these situations there has been urinary retention which leads to early attainment of the bladder threshold and hence frequent voiding. If the retention is marked, the patient may quickly reach a level of bladder distention which he is not able to control even if cortical inhibition is intact. Some of these patients, however, with only moderate retention, plus some loss of cortical inhibition, will develop frequency and urgency incontinence.
4. Local infection of the urethra, bladder neck, or prostate secondary to long-term or short-term retention or previous catheterizations adds to the symptomatology of frequency and urgency which may lead to incontinence at night when loss of cortical inhibition is most marked, whether due to psychological factors or to inherent neurological interference in the pathway.
5. Immobilization in bed, use of bedpan in supine position, weakness of abdominal and diaphragmatic contraction, lack of effort in attempting micturition through relaxation of sphincter and use of accessory muscles, and poor and ineffective detrusor contractions contribute to incomplete bladder emptying resulting in retention with tendency to cystitis, frequency, and urgency incontinence.

Management

If acute retention occurs, catheterization should be done every 8 hours, and if voiding is not spontaneous within 24 hours, an indwelling catheter may be used. After the patient has been fully conscious for 5 to 19 days, the catheter should be removed. Retention is uncommon, but if over 90 cc. of residual urine persists, the catheter should be replaced until the urologic problem is resolved. In such cases, the catheter must be irrigated daily with a bacteriostatic solution, such as benzalkonium

(Zephiran) chloride (1:20,000), and changed weekly. When the patient is able, habit training and supervised timed voidings will develop control.

If incontinence is a problem, check for retention, and if it is over 90 cc., replace the catheter temporarily. If the residual is small, incontinence is on the basis of poor cortical inhibition, and the catheter may be replaced temporarily to await further neurological recovery. The general condition should make it possible to decide on the necessity for an indwelling catheter. If possible, unless retention with infection is present, use of the indwelling catheter should be avoided.

Loss of cortical inhibition manifests itself in most severe form by bowel and bladder incontinence. Bowel incontinence can usually be brought under control first, both on an active and on a passive basis. This is done by achieving a bowel regimen with daily daytime evacuation, with use of bedpan or commode with suppository or enema as needed.

Bladder continence is achieved by stressing urination every two to three hours, synchronized to the patient's spontaneous detrusor contractions during waking hours, with late evening catheterization to remove residual and minimize nocturnal incontinence. When no residual occurs catheterization can be discontinued.

Trials without the catheter should be repeated periodically until the patient can do without or until neurological recovery has reached its zenith. If recovery has been poor and the patient still has urologic difficulty, prolonged catheter drainage (if there is a high residual of urine) or other device for incontinence, such as a rubber urinal, may be necessary. If recovery has been good but urologic difficulty persists, treatment for any underlying or preexisting uropathology should be instituted. In men, transurethral prostatic resection may be needed in those with benign prostatic hypertrophy. In women, urethral dilatation and local therapy to the bladder and urethra (nitrofurazone [Furacin] urethral suppository or dilute silver nitrate) may be helpful in cicatricial urethritis.

Parasympathicolytic drugs (such as methantheline [Banthine] bromide) are of little value usually when incontinence results from lack of cortical control rather than muscular hyperactivity, but they may be of symptomatic value in frequency secondary to low-grade infection. In this case, primary attention should be on culture of organisms and appropriate antimicrobial agents.

In all cases, after catheter removal, begin a supervised habit training schedule of voiding every two to three hours, gradually lengthening the intervals as recovery permits. Continual reorientation, encouragement, explanation, diminution of embarrassment, and use of sitting position, diaphragm, and abdominal muscles in voiding are essential in achieving urinary continence during recovery from loss of cortical inhibition.

With indwelling catheters, irrigate four times daily with sterile saline solution, boric acid, phosphoric acid, or half-strength G (Suby) solution. Also use ammonium chloride or methenamine mandelate (Mandelamine) to keep the urine acid. Change the catheter weekly, under sterile conditions. Intermittent prophylactic chemotherapy (full therapeutic dose for one week for each month) may be useful in lessening urinary tract infection.

Conclusions

The overwhelming cause of urinary incontinence was found to be loss of cortical inhibition, and urologic complications were usually secondary to this phenomenon. Frequency and dysuria frequently occurred as the result of preexisting vesical neck obstructive disease and/or infection. Recovery from loss of cortical inhibition usually followed in the following phases: bowel and bladder incontinence, bladder incontinence, nocturnal urinary incontinence, and normal bladder control.

The high incidence of incontinence among those hemiplegics who failed to achieve independent ambulation was noted in a prior study when the causes of failure to achieve independent ambulation were being evaluated. Despite the high incidence it is not felt to be a causative factor in itself.

Persistence of urinary incontinence is a poor prognostic sign, but it must be evaluated in terms of all other factors present. A few patients remained incontinent when they became ambulatory. In none of our patients was this considered the reason for failure to achieve independent ambulation by itself but it usually indicated organic mental changes, poor motivation, emotional problems, and/or severe neuromuscular involvement. In most situations where independent ambulation was not achieved, the patient had not only bladder incontinence but also bowel incontinence.

Incontinence has been found to retard and impede achievement of independent ambulation because it causes difficulties in transportation and management of the patient in various clinics and gymnasiums and diminishes the enthusiasm and positive motivation of both the patient and the therapeutic team. Most instances of incontinence can be improved to the point of no interference with the rehabilitation treatment program through a habit-forming bladder program, positioning, encouragement, assistive abdominal and diaphragmatic contractions to achieve full bladder emptying, continued efforts at progressive physical activity and ambulation, a bowel training program with achievement of fecal continence, and the correction of local pathological situations in the urinary tract.

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D-PANTOTHENYL ALCOHOL IN MANAGEMENT OF PARALYTIC ILEUS

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The effectiveness of D-pantothenyl alcohol in the treatment of paralytic ileus was tested by comparing two groups of 50 patients after abdominal operations. Both groups received the customary postoperative care as seemed indicated by the attending surgeon, but in addition 50 patients received intramuscular injections of 250 mg. of D-pantothenyl alcohol every six hours until normal peristalsis was established, while the remaining 50 received a placebo in the same manner. In the group receiving the drug it was possible to discontinue the use of tubes and of venoclysis sooner than in the other group, but it was debatable whether the actual difference in the average case was of practical importance. The drug was used in 12 additional patients who had profound postoperative intestinal atony, and in each case it appeared to cause resumption of bowel sounds, passage of flatus, and relief from distention. No undesired side-effects were observed.

One of the distressing complications encountered after a surgical operation is adynamic ileus. Temporary paralysis of the intestine can result from direct injury to the intestine, chemical irritation, infection, reflex reaction to injury, and metabolic imbalances such as uremia and electrolyte deficiencies. Because of the serious consequences that may result from this complication, most surgeons today give considerable attention to its prevention. Modern practices of restoring good nutrition and blood volume before surgery, correction of electrolyte deficits, intestinal intubation, antibiotic preparation of the intestine, early ambulation, and other aids have helped in minimizing this syndrome.

Despite the infrequency of severe ileus, lesser degrees of intestinal paralysis are common. After any intra-abdominal procedure with its inherent trauma to the intestinal tract, a period of intestinal atony with mild distention may be expected. After this, many patients may have "gas pains" which usually herald the onset of intestinal peristalsis. The majority of patients then eliminate flatus and progress without incident to recovery of normal intestinal activity. For reasons that are not always clear, some patients have a delayed onset of peristalsis. They become distended and uncomfortable, necessitating the use of gastric suction, the rectal tube, enemas, and parasympathomimetic drugs. Most patients respond to these measures, but they are often physically exhausted by the regimen. Only the rare case is refractory and proceeds to true adynamic ileus. Any agent which would safely shorten the period of postoperative intestinal atony might decrease the discomfort due to the resumption of peristalsis and also be of value in the treatment of paralytic ileus. This study is an evaluation of an agent which may be useful in the prevention and treatment of paralytic ileus.

Review of Literature

D-Pantothenyl alcohol (Panthenol) is the alcohol of pantothenic acid, a vitamin of the B group. This vitamin, although included in most multi-vitamin preparations, has never been shown to be essential to human nutrition. It has been given to both animals and humans in very large doses with no toxic effects. Pantothenic acid is found in virtually every food eaten by man.

Early animal experiments demonstrated several interesting manifestations of pantothenic acid deficiency. McKibbin and co-workers[1] in 1940 described a deficiency syndrome in the dog which suggested to them a disorder of the parasympathetic nervous system. Bly and co-workers,[2] in 1943, using pantothenic acid-deficient dogs with jejunostomies, demonstrated a 50% decrease in intestinal motility and a 40% to 60% decrease in the absorption of carbohydrate and protein. Rats were fed a diet deficient in pantothenic acid by Jurgens and Pfaltz[3] in 1944 with the interesting finding of gas-filled atonic small intestines. This was alleviated rapidly by feeding pantothenic acid.

This latter study led Jacques[4] to use this vitamin in the treatment of adynamic ileus. He reported 16 severe cases with fecal vomiting that had not responded to all known therapeutic measures. Each patient was given 50 mg. of calcium pantothenate intramuscularly every three hours with uniformly good results. The passage of flatus, which Jacques considered the best sign of improvement, began 1½ to 13 hours after the initial injection. Banerji,[5] after reading Jacques' report, treated 19 patients with calcium pantothenate, with excellent results in 18. Favorable results in treating ileus with pantothenic acid were also reported by Zutelman,[6]

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Hofmann,[7] and Docherty.[8] The only report from the United States was by Bergman,[9] who treated 44 cases of ileus with favorable results. Felten [10] gave D-pantothenyl alcohol to 50 patients with severe gas pains, constipation, and distention after operation. He found that the majority expelled flatus in a few hours with marked subjective relief.

The uniformly good results reported seem to indicate that pantothenic acid is effective in restoring normal intestinal activity. The mechanism by which it exerts its effect remains unknown. Whereas pantothenic acid itself is not essential to nutrition, the discovery by Lipmann [11] of coenzyme A, which is a derivative of pantothenic acid, revealed the basic importance of the pantothenyl complex in cellular physiology. Coenzyme A is involved in the aerobic utilization of glucose, the synthesis of fatty acids, sterols, and steroids, and the acetylation of choline. It is this latter function which may be responsible for the action of D-pantothenyl alcohol in the intestinal tract.

Table 1.—*Type of Operations Performed on Fifty Patients Treated with D-Pantothenyl and Fifty with Placebo*

	Group 1, D-Pantothenyl		Group 2, Placebo	
Type of Surgery	No. of Cases	Av. Time to Pass Flatus, Hr.	No. of Cases	Av. Time to Pass Flatus, Hr.
Gastric	13	40	12	55
Laparotomy; intestine not involved	13	32	11	60
Biliary	9	34	8	63
Intestine resection and anastomosis	6	36	8	75
Intestinal obstruction	4	24	4	78
Peritonitis due to perforated viscus	3	36	4	91
Appendectomy	2	24	3	48
Total	50		50	

Materials and Methods

Group 1.—One hundred unselected patients undergoing various intra-abdominal surgical procedures were used as the primary group for this study. Each patient was prepared for surgery with the usual examinations and preliminary procedures. Identical multiple dose vials containing D-pantothenyl alcohol and a placebo were used. The identifying code was on a removable label. Material for treatment was supplied to the ward with only the patient's name, the code having been removed. A list of the patients and the agent used was recorded. The clinical observers were not aware of the nature of the drug being administered. Fifty patients received D-pantothenyl alcohol and 50 others the placebo. The initial dose was started in the recovery room immediately after each operation and was continued until normal peristalsis was restored. Dosage was standardized at 1 cc. or 250 mg. of the active D-pantothenyl alcohol every six hours intramuscularly; a similar volume of the placebo was administered.

Group 2.—A second group of 12 patients who developed varying degrees of postoperative intestinal atony were treated with 250 mg. of D-pantothenyl alcohol intramuscularly every six hours until normal peristalsis was established.

In a study of this type the most difficult aspect was the evaluation of subjective complaints in the face of the many variables inherent to the postoperative period. All patients were treated as seemed indicated by the attending surgeon. No measure was added or withheld from the patient because of this study. Intestinal tubes, enemas, and other aids were used as deemed necessary. As a measurable end-point indicating the desired effect of the drug, the time of onset of audible peristalsis and the time of passage of flatus were selected. These observations were usually made at 6-hour to 12-hour intervals.

Results

Group 1.—Of the 100 patients treated by the double blind control method, 50 patients received D-pantothenyl alcohol and 50 others the placebo. Comparison of these two groups reveals them to be similar in most significant clinical aspects, including age and sex. Since the factor most likely to affect intestinal motility in the postoperative period was the type and extent of the surgery performed, the similarity of both groups is compared in table 1. Such factors as the duration of the operative procedures, the type of anesthetic agent, and the general condition of the patient were recorded and found to be essentially similar in both groups.

The 50 patients receiving D-pantothenyl alcohol developed audible peristalsis in an average of 25 hours postoperatively as compared to 55 hours in the control group. The passage of flatus was noted at an average of 48 hours in contrast to 66 hours in the placebo group. Since the appearance of bowel sounds and the passage of flatus indicate a resumption of intestinal activity, the figures seem to reflect a shortening of the period of postoperative atony in the treated group. No patients in group 1 and six patients in the control group developed signs of early ileus in the late postoperative period.

Table 2 divides the patients in the treated and control groups into comparable age groups. The time required to pass flatus averaged at least 24 hours longer in the control group in each division. Age per se did not influence the period of postoperative atony in either group.

Since patients with intestinal surgery or peritonitis are most likely to develop intestinal atony, similar types of operative procedures are compared in table 1. Three patients with diffuse peritonitis due to perforated intestine were treated with D-pantothenyl alcohol with the passage of flatus in an average of 36 hours as compared to four patients in the control group with atony for an average of 91 hours. Resection of the intestine with anastomosis was accomplished in six patients treated with D-pantothenyl alcohol with the average time for passing flatus of 36 hours as compared with eight patients in the placebo group who required 75 hours to achieve the same result. In each group were four patients with mechanical intestinal obstruction relieved by operation. The four treated with D-pantothenyl alcohol were expelling flatus in an average of 24 hours, whereas the controls averaged 78 hours. The onset of peristalsis in the control group was similarly prolonged after gastric surgery, biliary surgery, appendectomy, and laparotomies for lesions not involving the intestinal tract.

Of the 50 patients treated with D-pantothenyl alcohol, only 1 developed nausea and vomiting. This case seemed to be a failure of treatment until obstruction of the gastroenterostomy stoma was demonstrated. After the obstruction cleared the patient proceeded to complete and rapid recovery. One patient undergoing a right colectomy had no peristalsis for four days but then progressed normally. In each of the 50 cases, after normal peristalsis returned, the patients continued to complete recovery with no later intestinal dysfunction.

Of the 50 patients treated with the placebo, 6 developed a recurrence of abdominal distention and absent bowel sounds after the usual period of postoperative atony had cleared. In three of these, gastric suction was reinstituted along with multiple enemas with clearing of the ileus within 48 hours. D-Pantothenyl alcohol, 250 mg. every six hours, was given to the other three after the drug code was broken. Two of these passed large amounts of flatus within 12 hours while the third was free of distention 36 hours after institution of therapy.

In evaluation of the more subjective data it was found difficult to grade symptoms. All patients complained of discomfort in the early postoperative period, but the majority in both the treated and control groups had minimal complaints after the first 24 hours. Complaints most often registered included abdominal soreness and discomfort from intestinal tubes and intravenous therapy. Nausea and vomiting were unusual after the immediate postanesthetic period. It was noticed that, once normal peristalsis returned, the patient usually felt better even when there were no specific complaints. In the treated group the earlier resumption of intestinal function allowed the earlier elimination of tubes and intravenous administration of fluids and thus in effect gave a measure of indirect subjective relief.

Group 2.—Of the 12 selected patients treated with D-pantothenyl alcohol because of profound postoperative intestinal atony, in each case abdominal distention, absent bowel sounds on auscultation, and marked subjective complaints such as abdominal discomfort, nausea, and fulness were present. These cases are presented briefly.

CASE 1.—A 12-year-old girl with a ruptured appendix had an appendectomy. Twenty-four hours after operation, marked distention with absent peristaltic sounds had developed despite intestinal suction. D-Pantothenyl alcohol was given, with resumption of bowel sounds after 3 hours and the passage of flatus after 12 hours. All distention had cleared and the patient felt greatly improved within 24 hours.

CASE 2.—A 22-year-old woman with acute pelvic cellulitis underwent exploratory laparotomy. Twenty-four hours after operation, marked distention was present and peristalsis was absent. Nausea and vomiting were severe. D-Pantothenyl alcohol was given, with the passage of flatus in 3 hours and clearing of all distention within 24 hours.

CASE 3.—A 30-year-old woman with carcinoma of the cervix had radical hysterectomy and lymphadenectomy. Twenty-four hours after operation, distention and a silent abdomen were noted despite intestinal suction. D-Pantothenyl alcohol was given with bowel sounds and passage of flatus within 12 hours. Normal peristalsis and a flat abdomen were noted within 24 hours.

CASE 4.—A 34-year-old man fractured his ribs on the left side. Three days after injury marked distention, a silent abdomen, and considerable discomfort had developed. Enemas, gastric suction, and rectal tubes had not helped. D-Pantothenyl alcohol was given, with the passage of flatus and subjective relief within 12 hours. All distention cleared within 24 hours.

TABLE 2.—*Age Distribution of Fifty Unselected Patients Treated with D-Pantothenyl and Fifty with Placebo*

	Group 1, D-Pantothenyl		Group 2, Placebo	
Age, Yr.	No. of Cases	Time for Passage of Flatus, Hr.	No. of Cases	Time for Passage of Flatus, Hr.
0-20	3	48	2	108
20-40	13	33	14	57
40-60	22	35	20	72
60-80	12	40	13	67
80 or over	0	...	1	60
Total	50		50	

CASE 5.—A 25-year-old man with intestinal obstruction secondary to adhesions after gastrectomy had lysis of adhesions. Three days after relief of the obstruction, the abdomen became markedly distended with hypoactive bowel sounds. A recurrent obstruction was suspected. D-Pantothenyl alcohol was given, with resumption of active bowel sounds and passage of flatus within 12 hours. All distention cleared within 36 hours with complete subjective relief.

CASE 6.—An 89-year-old woman with obstruction of the large intestine underwent loop colostomy followed by right colectomy. On the ninth day after the colectomy, bowel sounds disappeared and the abdomen became markedly distended and silent. It was feared that reintubation would be necessary. D-Pantothenyl alcohol was given, with the return of bowel sounds within a few hours, and flatus with a large bowel movement within 12 hours.

CASE 7.—A 31-year-old woman had tubo-ovarian abscess with peritonitis and underwent salpingectomy. Thirty-six hours after operation, marked distention, nausea, vomiting, and absent bowel sounds were noted. D-Pantothenyl alcohol was given followed within 6 hours by the explosive passage of flatus with clearing of distention within 24 hours.

CASE 8.—A 52-year-old woman with intestinal obstruction due to adhesions had lysis of adhesions. On the fourth day after surgery, distention was marked, with a silent abdomen. A single dose of D-pantothenyl alcohol was given with the passage of flatus in three hours followed by a bowel movement that evening.

CASE 9.—A 41-year-old woman with pelvic inflammatory disease had a hysterectomy. On the seventh postoperative day the patient developed fever, a silent abdomen, and distention. D-Pantothenyl alcohol was given with the passage of flatus within 3 hours and clearing of the ileus within 24 hours, even though her fever persisted until an abscess was drained four days later.

CASE 10.—A 40-year-old woman with carcinoma of the cervix had radical hysterectomy and lymphadenectomy. Thirty-six hours after operation she developed marked distention, with a silent abdomen. D-Pantothenyl alcohol was given with the passage of flatus within a few hours. The patient felt better within 24 hours, but 48 hours were required for the distention to clear completely.

CASE 11.—A 25-year-old woman with cholelithiasis had cholecystectomy. On the second day after operation she became distended, with no bowel sounds. D-Pantothenyl alcohol was given, with resumption of peristalsis within 12 hours and the passage of flatus within 24 hours.

CASE 12.—A 66-year-old woman with carcinoma of the ovary underwent total hysterectomy. Twenty-four hours after operation, marked distention and absence of bowel sounds developed. D-Pantothenyl alcohol was given, with resumption of good bowel sounds and the passage of flatus within 24 hours. All distention cleared within 48 hours.

In each case, D-pantothenyl alcohol appeared to produce a significant effect, although it was recognized that at least some of these patients might have improved spontaneously as rapidly without the drug. Further studies are needed, but the above cases are considered to be conclusive enough to treat subsequent cases of postoperative atony with this agent.

Side-effects.—Side-effects from the administration of D-pantothenyl alcohol could not be demonstrated. There was no complaint of excessive abdominal cramps, tachycardia, and flushing as is so often noted with parasympathomimetic drugs. At no time could symptoms be elicited due to an overdosage of the drug. No evidence of sensitivity, such as a rash, unexplained fever, or angioneurotic edema, was seen.

Comment

The inherent difficulty in evaluating any drug on the basis of clinical observation was apparent during this study. This difficulty was magnified during the postoperative period when so many variables were present, each affecting the well-being of the patient. It was felt, however, that this study represented an adequately controlled clinical evaluation.

D-Pantothenyl alcohol given in the immediate postoperative period appears to facilitate the resumption of normal peristalsis after operative procedures within the abdomen. It is debatable whether the actual difference in the average case is one of practical significance. The over-all difference demonstrated would not necessarily warrant the routine use of this drug in unselected cases. On the other hand, in the control group there were six patients who developed signs of early ileus in the late postoperative period who might not have had this difficulty if D-pantothenyl alcohol had been administered routinely. The prophylactic use of D-pantothenyl alcohol might be indicated in that group of patients in whom the type and magnitude of intestinal surgery is conducive to the development of paralytic ileus.

D-Pantothenyl alcohol gave excellent results in the 12 patients in group 2 treated for moderately severe intestinal atony as well as in 3 patients who developed distention after receiving the placebo. These findings are in agreement with the experience of other investigators. It would seem that D-pantothenyl alcohol is definitely indicated in those patients who appear to be developing postoperative distention. Certainly those patients with fully developed atony or classic adynamic ileus should be given the benefit of D-pantothenyl alcohol therapy.

The use of this drug is made more attractive by its apparent lack of toxicity as demonstrated both in this study and in the experience of others. The complete absence of abdominal cramps with tachycardia and flushing so often noted after the administration of a parasympathomimetic drug was striking. The most likely theory as to the reason for its effectiveness is that it stimulates the formation of acetylcholine through the coenzyme for acetylation (coenzyme A) of which pantothenic acid is a component. Thus the mode of action is through the "normal mechanism" controlling intestinal activity. The hesitation of many surgeons to use prostigmine-like drugs is often due to the fear that violent peristalsis might do damage to the operative site. D-Pantothenyl alcohol appears to be a safe yet effective agent capable of stimulating peristalsis and preventing paralytic ileus.

Summary and Conclusions

D-Pantothenyl alcohol and a placebo were administered alternately to 100 unselected patients undergoing intra-abdominal surgical procedures, utilizing the double blind control method. D-Pantothenyl alcohol appeared to shorten the duration of postoperative intestinal atony. Twelve other patients with moderately severe paralytic ileus were treated with D-pantothenyl alcohol. Within 24 hours, all 12 patients had resumption of peristalic activity as indicated by audible peristaltic sounds, the passage of flatus, and marked subjective relief. All distention had cleared within 48 hours. D-Pantothenyl alcohol appears to be a safe yet effective agent capable of stimulating peristalsis and preventing paralytic ileus.

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DISCOVERY OF TYPHOID CARRIER BY SEWAGE SAMPLING

Lois Ann Shearer, M.P.H., Alcor S. Browne, Ph.D., Robert B. Gordon, M.D.
and
Arthur C. Hollister Jr., M.D., Berkeley, Calif.

A method was applied for the bacteriological sampling of sewage through manholes at crucial points in an urban sewerage system in order to locate carriers of typhoid. The map shown here gives the arrangement of sewers in a city of 2,200 population where four cases had occurred in five years. The sampling method narrowed the field of inquiry to a small area, and bacteriophage typing of the Salmonella obtained yielded the final clue that led to identification of the carrier. The most significant advantage of this method is the ability to locate a carrier by use of a practical field study technique when the usual epidemiologic methods have failed.

In 1948, 1950, and 1952 Moore and his associates[1] reported the successful finding of typhoid and paratyphoid carriers by the continuous sampling of sewage for the presence of Salmonella. In their method, they suspended gauze strips (referred to as swabs) in the sewage flow and periodically removed and cultured them for Salmonella. Beginning at major sewage collection points, such as sewage treatment plants, they followed, as a consequence of positive findings, the source of organisms through lateral sewers to the homes of the carriers. Similar studies have been reported by a number of other investigators.[2] This sewage sampling procedure represents a new approach to the problem of locating carriers of enteric and other diseases in which the causative agent is present in the excreta. It also provides the epidemiologist with what appears to be an extremely valuable methodological tool.

Epidemiologic searches for carriers of enteric disease traditionally have followed a pattern of contact interviewing and analysis of the blood and excreta of suspected individuals. This method, although generally effective, has several drawbacks: 1. It may require a large number of trained field and laboratory workers. 2. Large numbers of specimens frequently must be obtained and processed before a positive finding is made. 3. People in the community are annoyed and sometimes alarmed by this type of investigation. Some individuals, especially those who have reason to believe that they themselves may be carriers, often refuse to cooperate. 4. A not unusual situation is the inability to locate the carrier by traditional epidemiologic methods in spite of repeated outbreaks of typhoid.

For some time the California State Department of Public Health has been interested in the swab technique. An opportunity to study and utilize the

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From the Bureau of Acute Communicable Diseases (Miss Shearer, Drs. Gordon and Hollister), and Bacteriology Laboratory (Dr. Browne), California State Department of Public Health. Dr. Gordon is now in the Department of Orthopedic Surgery, New York University, Bellevue Medical Center, New York.

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A method was applied for the bacteriological sampling of sewage through manholes at crucial points in an urban sewerage system in order to locate carriers of typhoid. The map shown here gives the arrangement of sewers in a city of 2,200 population where four cases had occurred in five years. The sampling method narrowed the field of inquiry to a small area, and bacteriophage typing of the Salmonella obtained yielded the final clue that led to identification of the carrier. The most significant advantage of this method is the ability to locate a carrier by use of a practical field study technique when the usual epidemiologic methods have failed.

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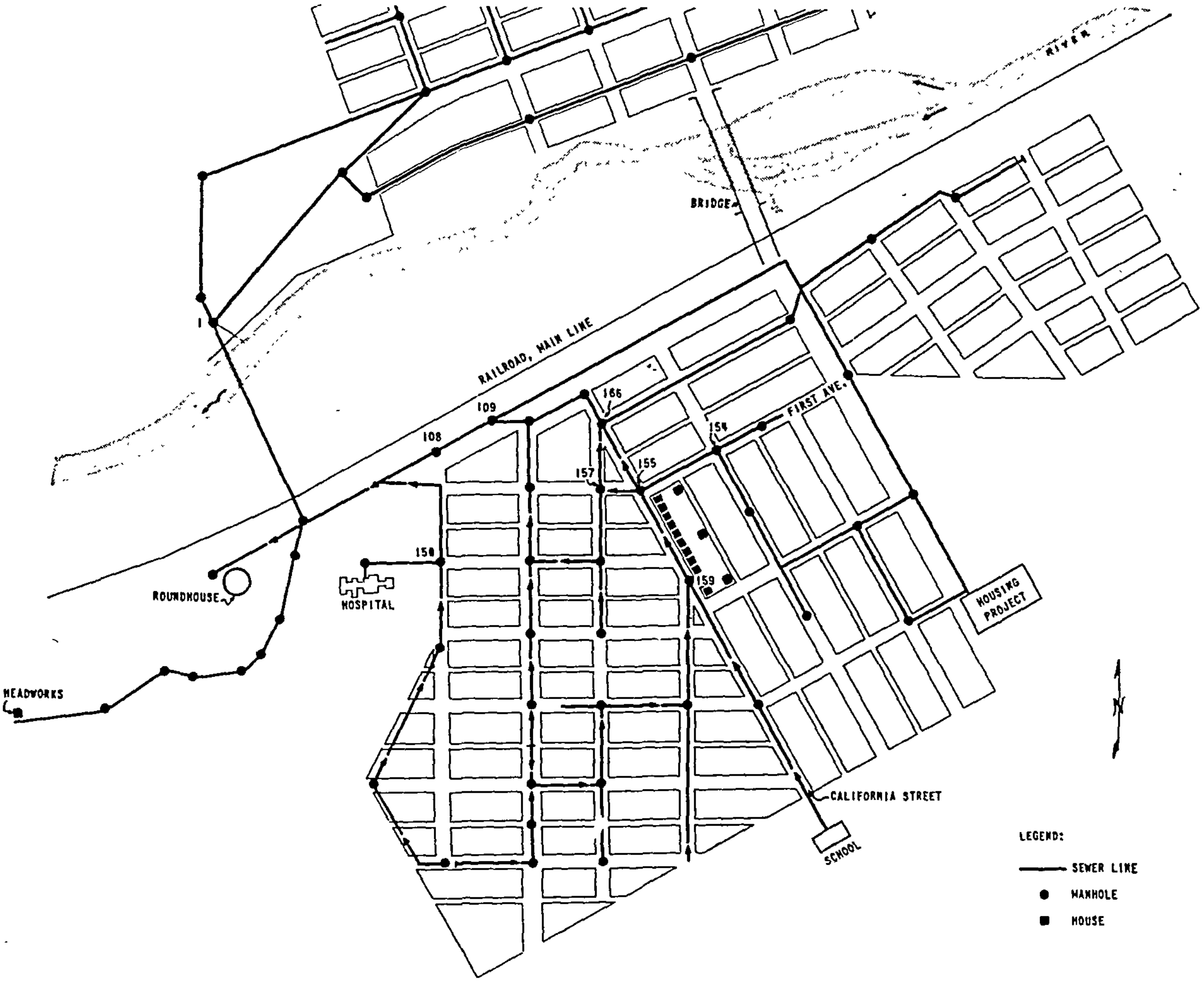
sewage sampling method was presented to the department in the summer of 1956. In and near a city of 2,200 population in the High Sierra country of California, a small but intermittent number of cases (four in five years) of typhoid had been reported over the preceding several years without discovery of the source of the infection. Because of the cooperation offered by the local governing and health officials and an engineering knowledge of the sewer system, it was felt that this community represented an excellent site for such a study. The major industries were railroading and lumbering. In addition, because of the plans to develop this community into a resort center, it was felt advisable to locate the possible carriers with as little contact as possible with the general public. A team consisting of physicians, nurses, microbiologists, and sanitary engineers was formed to make this study. The epidemiologic story is recounted here. Details of specific laboratory techniques will be reported elsewhere.[3] The sanitary engineering aspects have been reported by Greenberg, Wickenden, and Lee.[4]



Map of principal sewer lines and manholes in city where sewage sampling was done and discovery made of typhoid carrier.

Method of Study

Since there was no information available which would suggest the area in which the carrier (or carriers) resided, it was necessary to hold the entire town suspect. Even this assumption was somewhat dubious since the possibility could not be ruled out that the source of the cases was an itinerant, possibly a railroad worker. Preliminary work consisted of studying maps of the sewage system of the city and locating and opening certain manholes which appeared to be in key locations. Difficulties were encountered in finding some of the manholes which were covered with earth or asphalt. In these cases, a mine detector was used to locate the manhole. Other manholes were "dry," a result of obstructions in the lines, while others which were on the maps apparently did not exist at all.

When the preliminary work was completed, a mobile bacteriological laboratory was brought to the site of the investigation. Swabs consisting of pieces of fine mesh surgical gauze folded into eight thicknesses, 6 in. long by 4 in. wide, were prepared. These were attached to strings and placed in the sewage stream at manholes which were selected to provide a survey of the Salmonella content of the entire sewage system. The figure shows the principal sewer lines and location of manhole 108. The swabs were removed after 48 hours and taken to the mobile laboratory where they were examined by the method of Moore and co-workers,[1c] as modified by the Division of Laboratories of the California Department of Public Health.

On July 9, only three days after the sampling began, a culture positive for Salmonella typhi was obtained from the head works (see figure) of the sewage system. While it had no value for localization, it was encouraging to know that there was probably a typhoid carrier in the community and that the method was capable of detecting his presence. There were no further findings of S. typhi until July 14, on which day the swab in manhole 157 yielded a positive culture. A day later, July 15, the swab in manhole 108 was found to be positive, and on July 16 positive cultures were obtained from manholes 109 and 166. During this period daily swab samples were collected from selected manholes in the northern portion of the city and from manhole 1, through which the entire sewage flow from that part of the city passed. These swabs were consistently negative and as a result further work was limited to the southern portion of the city, although surveillance was maintained at manhole 1.

When the presence of a typhoid carrier had been indicated, the field investigation was suspended temporarily, so that further plans could be developed for research purposes and additional characterization of the organism which had been found could be obtained.

Phage typing, which was considered essential, was attempted in our laboratory by multiple pickings from each culture, but the organisms were found to be "untypable" by phages at our disposal, although they all appeared to be identical and to belong to group D. Cultures were then submitted to Dr. Philip R. Edwards of the Communicable Disease Center of the United States Public Health Service in Atlanta, Ga., who reported all organisms to be members of phage group D. However, in addition to the lysis of phages which placed the cultures in group D, the cultures were lysed by a phage identified as Utrecht 9 described by Scholtens.[5] This phage type had been found by Scholtens in two epidemics and a few isolated cases in Holland and is not known to have been reported from any area in the United States. In view of this successful typing, a culture isolated from an acute case of typhoid in the area during the previous year and reported then as "untypable," was resubmitted to the Communicable Disease Center. Interestingly enough, it was also typed by Utrecht 9. After the clinical illness this patient had been released from surveillance with a negative stool culture. At the time of the study, control swabs were placed in the manhole outlet through which sewage flowed from the household of this known ex-case. All of these swabs were negative.

In August the field crew and mobile laboratory returned and active sampling was resumed. On the 5th, 6th, 16th, 17th, and 18th of August, the swab from 156 was positive for S. typhi. On the 16th, swabs from manholes 157 and 155 were also positive. As seen from the figure, the sewage from the hospital and part of the southwest section of the city passed through manhole 156. The flow from this manhole, as demonstrated by placing dye in the hospital sanitary system, is direct to the main line of the sewer system.

Swabs from manholes 159 and 154, both of which drained into 155, remained negative while under constant surveillance. This tended to place the carrier somewhere in the immediate drainage area of manhole 155, which is the most distant point in the system from which positive findings were obtained. Swabs were then placed in manhole 155 in such a manner as to get separate samples of the flow from the two feeding sewers. The swab from the California Street sewer was positive while the swab on First Avenue remained negative. This further located the carrier on California Street between manholes 155 and 159, which area involved only the small group of homes shown on the map.

Since the phage type identified had previously been reported only from Holland, we attempted to determine if anyone from this block had resided in Holland and/or had symptoms of typhoid. A roster was prepared of patients and staff present in the hospital during the period that positive findings were obtained in manhole 156. This was compared with the list of people living in the suspect block. One individual was found to have a common link and to fit this pattern. Inquiry then revealed a 77-year-old retired railroad worker who had been in the hospital for the treatment of hypertension and congestive heart failure during the period that typhoid had been isolated from the hospital manhole and who also lived in the suspected residential area. During his hospitalization he was treated for cardiac disease, but his role as a typhoid carrier was not suspected. He came to this country from Germany 50 years ago and both before and after had traveled extensively as a sailor. While in Germany he had lived in the same house with a person from Holland who was known to have typhoid. The patient stated, however, that he had never had any symptoms of the disease himself. Stool specimens were obtained from him and readily yielded S. typhi, of the same phage pattern as the cultures isolated from the sewers, thus confirming him as the carrier being sought. The carrier was hospitalized Aug. 3 to 18. In view of the evidence presented by Harvey and Phillips [2a] that S. paratyphi B may survive for periods of 10 weeks in sewers in the absence of contamination, a positive sample from 155 on the 16th was considered possible.

Comment

One of the principal advantages of the method presented herein is the localization of carriers of enteric disease without invasion of the household or of the privacy of individuals and without undue public alarm. Just how far it is possible to proceed in localizing individual carriers depends on such variables as the construction of sewer systems and access to manholes. In Sidmouth, England, where Moore [1a] made his studies, it was possible to place swabs in access holes of individual house drains, thereby localizing the source to individual houses. On the other hand, presence of houses with individual privies or cesspools would preclude such a method of mass surveying, unless, of course, there was seepage into a stream or other body of water which in turn could be tested by the swab technique.

In this study it was felt that the practical limit of usefulness of the sewer system survey had been reached when the carrier was localized to one block. However, at this point, several methods for the further pinpointing of the source without any intrusion upon the population were apparent. The first and most attractive of these alternatives was previously described; the utilization of the limited geographical distribution of the phage type of the isolated organism. Although phage typing is an essential part of an epidemiologic study of a typhoid outbreak, this to our knowledge is the first time that the phage type presented the clue that led to the presumptive description of the carrier.

Another procedure was considered but not found necessary to use in this particular situation. This would have been to pass a line to which was attached a number of swabs through the sewer in the direction of sewage flow so that one swab rested in front of each house. By withdrawing the line at the insertion point it should have been possible to detect the house which presumably was the source of the Salmonella, since it should be at the point of the first positive swab on the line. Should all indirect methods have failed it would, of course, have been possible to interview and collect stool specimens from the individuals in the limited number of suspected houses. Similarly, swabs could have been placed in individual toilets, then collected and cultured, as was done by Kwantes and Speedy.[6] This was actually performed in the town after the conclusion of the major portion of the project, and positive findings showed that this too would have been epidemiologically feasible.

Since this project was initiated as a study in methodology, other problems were investigated. One was to determine if grease which commonly accumulates on the insides of the sewers could act as a trap for the typhoid organisms, as has been suggested by Harvey and Phillips [2a] and by Browne and Greenberg.[7] The latter found that an appreciable number of sewer grease samples which had been washed up on beaches near sewer outfalls were contaminated with Salmonella. Accordingly, samples of floating grease, as well as "wipes" of the walls of accessible pipes, were obtained. A significant number of positive findings were made by this method, especially by the wipes. Further studies are under way on the value of direct grease sampling. If this proves successful it would eliminate the time and labor necessary for placing and removing swabs. It would also serve as an index of the Salmonella present in the sewer prior to the start of the studies.

Another question which was studied was the possibility of sending the samples directly to the State Central Health Department Laboratory, in this case 200 miles from the site. Duplicate swab samples were taken and one was analyzed in the mobile laboratory while the second was shipped by express to Berkeley in a portable icebox. On only one of the 275 duplicate samples submitted did the two laboratories differ in their findings.

Summary

A study was made of the feasibility of searching for typhoid carriers by culturing samples of sewage taken at different points within a city. In this instance, it was possible to localize the residence of a carrier to a single block. Further localization was rendered unnecessary when positive specimens were found in the sewage outflow from the community hospital and the name of a resident of the suspected block was found in the hospital roster. Direct stool cultures from this man showed him to be a typhoid carrier, and phage typing of the organisms indicated that he probably had acquired his infection many years previously in Europe. Localization was also accomplished by household toilet swabs. The method has proved feasible as a practical field study technique.

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FAILURE OF PENICILLIN IN TREATMENT OF ACUTE GONORRHEA IN AMERICAN TROOPS IN KOREA

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The results of treating patients with acute gonorrhea by five daily intramuscular injections of 600,000 units of procaine penicillin G were followed up in 148 men. The treatment failed in 30. In 13 of these a second course was given. It was successful in nine, and in the four cases of failure cure was obtained with oxytetracycline. In 17 men the initial course of penicillin which failed was followed by treatment with oxytetracycline; this was successful in 15 cases, and in the 2 men who were not cured by it treatment with chloramphenicol was successful. Two cases of failure of penicillin are cited to illustrate the course of the infection. The present high rate of failure with repeated doses is in marked contrast to the much lower rate of failure with single smaller doses reported elsewhere two years ago. This evidence that a penicillin-resistant strain of Neisseria gonorrhoeae has emerged is of grave significance.

The remarkable response of gonorrhea to penicillin has long been emphasized, and it is usually held that penicillin-resistant Neisseria gonorrhoeae do not appear. However, in Korea failure of gonorrhea to respond to an adequate course of penicillin treatment is not uncommon. Not infrequently, military physicians in Korea encounter in soldiers cases of acute gonorrhea which persist in spite of 5 or even 10 daily injections of 600,000 units of an aqueous solution of procaine penicillin G.

Materials and Methods

This paper is a report of failures of penicillin therapy in cases of acute gonorrhea among United States troops in Inchon, Korea. Inchon is a major Korean port with about 2,000 military personnel, nearly all Army, receiving medical care from the Army dispensary. The study covers a three-month period, from Jan. 1 to April 1, 1958, during which 165 cases of acute gonorrhea in these troops were treated. An adequate follow-up study was possible in 154 cases, and this is the number of cases analyzed. Since the only reason for inadequate follow-up study was the movement of patients to another area, discounting these cases should not bias the results.

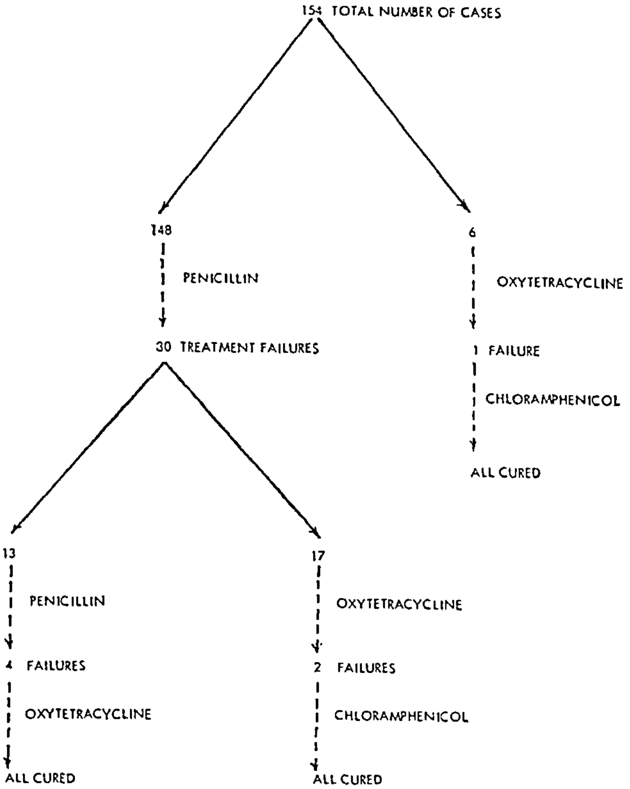
All cases represented acute gonorrhea with sudden onset of a purulent urethral discharge. In every case a history of recent sexual intercourse was obtained. Eight patients in this series had two cases of gonorrhea during the three-month period; therefore, a total of 146 persons were involved. These eight cases were felt to be reinfections and not treatment failures, since all of the patients had been asymptomatic for a period of at least two weeks after completing treatment and in seven of the eight a history of sexual intercourse after treatment was elicited.

Diagnosis.—The diagnosis of gonorrhea was made by the demonstration of characteristic biscuit-shaped, gram-negative, intracellular diplococci in Gram-stained urethral smears. All smears were examined by the same experienced technician. Smear findings in all cases of failure of treatment were confirmed by myself.

Treatment.—All patients with gonorrhea were given a printed sheet of directions and also instructed verbally to (1) be sure to take all five injections of penicillin, (2) return for reexamination three days after the last injection, and (3) abstain from alcohol and intercourse for two weeks. They were also given two weeks of medical restriction to their compound. No restrictions of other physical activities or exercise were imposed.

Except for those with a history of penicillin allergy, all patients received five daily intramuscular injections of 600,000 units of an aqueous suspension of crystalline procaine penicillin G. Only penicillin well within the expiration date was used.

Patients allergic to penicillin received a course of oxytetracycline therapy, 500 mg. four times a day for four days and then 250 mg. four times a day for three days. Patients treated with chloramphenicol were given 500 mg. four times a day for four days.



Type of treatment and results in 154 acute cases of gonorrhea.

Follow-up Study.—In order for the results of therapy to be evaluated, patients were entered on an injection record and this was checked daily for missed injections. Patients who failed to take the injections were called in and scheduled for additional injections to give a total of five treatments.

Any patient who was asymptomatic and free of discharge on examination three or more days after his last injection was considered cured. If a slight discharge persisted, at least two and usually three smears on different days had to give negative findings for N. gonorrhoeae before the patient was considered cured.

Results

The type of treatment and the clinical results are illustrated in the figure. In one of the six patients receiving oxytetracycline a relapse occurred and a course of chloramphenicol therapy was required for cure. Of 148 persons who received penicillin, 30 were not cured.

These 30 patients in whom penicillin treatment failed were divided into two groups, with 17 receiving oxytetracycline and 13 given a second course of penicillin therapy. Of these 13, 4 were not cured by this second course. They subsequently responded to a course of oxytetracycline therapy. In the group of 17 treated with oxytetracycline, 2 were not cured. Both were successfully treated with chloramphenicol.

In none of the 30 patients in whom penicillin treatment failed could a history of further sexual contact be obtained, even with careful inquiry. In two cases some doubt remained as to whether reinfections rather than treatment failures had occurred, since the interval between the last injection and the finding of a smear positive for N. gonorrhoeae was 11 and 13 days, respectively—considerably longer than in the other instances.

In the other 28 patients the time between the last injection and demonstration of positive smear results varied from zero to eight days, with an average of four days. In 14, N. gonorrhoeae was demonstrated in the smear zero to three days after the last penicillin injection. This interval could probably have been reduced somewhat with closer follow-up examinations of patients, since not infrequently a discharge had been present for a few days before the patient reported it.

Failure to receive all penicillin injections cannot account for the 30 instances of relapse, since only two patients missed one injection while two others missed two injections. These injections were made up, but a lapse of one or two days in the course of treatment in these four patients did result.

One interesting observation in the patients in whom penicillin treatment failed was that the character of the discharge often changed from thick and purulent to relatively thin and mucoid. The clinical picture changed from that of acute gonorrhea to one resembling nongonorrheal urethritis or chronic gonorrhea. Also, not infrequently a smear done early in the stage of treatment failure would be negative, while on repeat smear a day or two later myriads of typical intracellular diplococci would be apparent.

In 140 of the cases it was possible to examine the charts one month later for complications. There were eight penicillin reactions, an approximate incidence of 5%. All of them were mild, the chief manifestation being urticaria. Nongonorrheal urethritis occurred in 16 or about 10% of the cases. Additionally, there were two cases of epididymitis, one of prostatitis, and one of sterile injection site abscess.

Report of Cases

In most of the patients with treatment failure the discharge disappeared after one or two injections, only to return after treatment had been completed. The following case is typical.

CASE 1.—An 18-year-old boy was seen on Jan. 29, 1958, with a purulent urethral discharge which had begun the day before. He had had frequent sexual contacts, the most recent being four days previously. A smear proved positive for N. gonorrhoeae, and he was given a course of penicillin therapy. Three days after his last injection he reported with a small amount of moderately thick discharge. He denied further intercourse. Check of injection records revealed he had received all five injections. He stated that the discharge stopped on the second or third day of treatment but returned two days after his last injection. The smear was positive for N. gonorrhoeae. He was given a second course of penicillin treatment, and a final examination two weeks later revealed him to be asymptomatic and free of discharge.

In some of the failures the discharge diminished but did not disappear under treatment. In a few of these cases it was possible to demonstrate N. gonorrhoeae in the discharge while the patient was undergoing treatment. Details in one of these cases are given below.

CASE 2.—A 23-year-old man reported with a purulent urethral discharge on Feb. 10, 1958. He had been stationed in Korea since May, 1957, but had had no previous venereal disease. The discharge began the evening before, sexual intercourse having occurred six days previously. A smear was positive for N. gonorrhoeae. A course of penicillin therapy was prescribed. He returned on the fifth day of treatment with a persisting discharge which was positive for N. gonorrhoeae. He had received all five injections. He was given an additional five days of penicillin therapy. On the 10th day of penicillin treatment (Feb. 19), he reported that his urethral discharge had not disappeared. Smear revealed numerous pus cells and extracellular gram-negative diplococci but no intracellular forms. A repeat smear the next day was positive for N. gonorrhoeae. A course of oxytetracycline therapy promptly cleared his discharge. A final examination 18 days later (March 10) revealed him to be asymptomatic and free of discharge.

Comment

A 20% treatment failure rate is both unusual and unsatisfactory. Gjessing[1] reported a relapse rate of only 2.9% in 1,115 male patients with acute gonorrhea treated by the venereal department of the Bureau of Public Health, Oslo, Norway. A single injection of 300,000 units of procaine penicillin G was employed. In a series of 424 men treated similarly by the venereologic outpatient department of Marselisborg Hospital, Aarhus, Denmark, Nørgaard[2] reported 5% as having recurrences. Lodin[3] noted one recurrence among 78 Swedish male military recruits treated in the same way.

In the studies cited above the treatment failure rate varied from 1 to 5%; yet, although we used 10 times as much penicillin, 20% of our patients were not cured. That individual variation in penicillin metabolism, exercise, and alcohol consumption cannot account for this discrepancy is clear, since all these series involve mainly young males treated as outpatients.

The question that arises is whether these cases represent gonorrhea or some other disease. That is, how accurate is our diagnosis? The fact that bacterial culture studies were not done will no doubt be held, by some, as contributing to failure to establish the diagnosis. In males the finding of typical gram-negative intracellular diplococci is a practically absolute diagnostic criterion.[4] As Pelouze[4] and others have pointed out, all these criteria must be rigidly adhered to, since urethral exudates are frequently filled with extracellular, and even occasionally intracellular, cocci other than N. gonorrhoeae. To insure a correct diagnosis, I insisted that only a smear showing intracellular, gram-negative diplococci, of typical morphology, could be labeled as positive for N. gonorrhoeae.

Without a doubt, cultures would have been helpful. But the value of cultures for N. gonorrhoeae in a male is not to confirm a positive smear but to detect those cases of gonorrhea which yield a negative smear. Therefore, any error introduced by relying only on smears would give a falsely low value for the number of treatment failures. In an attempt to overcome this handicap, repeated smears were done on post-treatment discharges which were negative for N. gonorrhoeae at the first follow-up smear. However, no doubt an occasional case of post-treatment discharge labeled as nongonorrheal urethritis may have been an undetected treatment failure.

If, indeed, the treatment failures represent persistent gonorrhea, what evidence is there that these are not reinfections? It is, of course, impossible to prove that reinfection could not have occurred in each and every treatment failure. In order to rule out reinfection as far as possible, all patients were restricted to army compounds for two weeks and carefully questioned regarding further sexual contacts. Patients with gonorrhea are quite anxious while undergoing treatment, and, for a short while at least, follow instructions. These considerations do not rule out the possibility that an occasional treatment failure was the result of reinfection. However, they do eliminate reinfection as an explanation for the 20% failure rate.

It should be pointed out that reinfection cannot possibly explain treatment failures in patients in whom N. gonorrhoeae was demonstrated in the discharge while the patient was on penicillin treatment. The daily dose of penicillin used is several times as great as the amount needed for effective prophylaxis of gonorrhea.

Failure of penicillin in the treatment of gonorrhea is a common experience in the Far East. The chief of the urology service at the U. S. Army's

121 Evacuation Hospital in Korea has frequently encountered penicillin treatment failures.[5] Kern[6] reported nine failures in 59 consecutive cases of gonorrhea treated in the port city of Pusan, Korea. Treatment was identical with that used in this study. Sabath[7] had a failure rate of over 30% among troops in the First Cavalry Division area in Korea treated with three daily injections of 600,000 units of procaine penicillin G in oil with 2% aluminum monostearate.

It seems to me that these cases of penicillin treatment failures can only be explained on the basis of penicillin-resistant strains of N. gonorrhoeae. When referring to penicillin resistance, increased relative resistance is meant. That is, a significantly higher concentration of penicillin is required for an antibacterial effect than is the case with usual strains of N. gonorrhoeae. Surprisingly, until recently there were practically no reports on penicillin-resistant N. gonorrhoeae in the literature.

From Great Britain, King[8] reported in March, 1958, "There is evidence that penicillin-resistant strains of gonococci are now emerging. Some cases of acute gonorrhœa fail to make any response to doses of penicillin which in the past were nearly always highly efficacious. Repeated doses of penicillin and doubling the doses may have no effect. In other cases, response seems satisfactory but relapse follows within a day or two. Quantitative in-vitro tests for sensitivity to penicillin suggest that in these cases organisms from the secretions are considerably less sensitive to penicillin than the Oxford staphylococcus or other strains of gonococci."

Cradock-Watson and co-workers[9] noted an apparent increase in penicillin treatment failures in England in a recent report of 200 cases. In vitro sensitivity studies, when compared to the clinical results, showed most of the failures to be in the relatively small group of patients who were infected with the more penicillin-resistant strains.

Bernstein[10] recently completed a thorough study of the bacteriology of penicillin treatment failures among United States military personnel in Japan. He demonstrated in vitro resistance of certain strains of N. gonorrhoeae to penicillin. Furthermore, the results of these in vitro sensitivity studies, when combined with blood penicillin level determinations, correlate well with the clinical course of the patients with penicillin treatment failures. He has shown that those in whom penicillin treatment has failed can be cured with penicillin providing it is administered in doses which raise the blood penicillin level sufficiently to overcome the penicillin resistance of N. gonorrhoeae. Bernstein also considers the repository form of penicillin to be of little value, since it does not raise the blood penicillin level sufficiently.

Although many authorities recommend treatment of acute gonorrhea in the male with a single injection of 600,000 units of repository penicillin, this has been abandoned by most military physicians in Korea. I have found procaine penicillin G in oil with 2% aluminum monostearate disappointing. Not only are treatment failures more common, but the clinical picture is obscured by the more prolonged suppressing action of the repository form of penicillin.

In this study, oxytetracycline was used a total of 23 times, with three failures. I believe that these failures are due to resistance of N. gonorrhoeae rather than to the patient's failure to take the medicament. When used in amounts of 2 Gm. daily, in divided doses, broad-spectrum antibiotics not infrequently fail to cure when penicillin treatment has failed. Others have had the same experience, even though this treatment was continued for seven days.[11] Although, in my experience, chloramphenicol had cured about 10 times when penicillin had failed, Romsey,[5] as well as Bernstein,[10] have reported occasional failures with chloramphenicol.

From the clinical standpoint, the emergence of penicillin-resistant strains of N. gonorrhoeae has grave significance. No longer can acute gonorrhea be considered lightheartedly as a disease with a certain cure and less disability than a common cold. The twin problems of chronic gonorrhea in the male and the asymptomatic male carrier, which had been largely banished by penicillin, have returned. It is probably only a matter of time until penicillin resistance will be met on an increasing scale all over the world. Furthermore, careful and prolonged follow-up studies will be necessary. In all likelihood various types of "provocative" tests will again have to be performed to ascertain a cure.

Summary

Among a series of 146 male military personnel treated for acute gonorrhea in Inchon, Korea, 30 (20%) failed to be cured by a course of five daily injections of 600,000 units of crystalline, aqueous, procaine penicillin G. It is felt that increased penicillin resistance on the part of Neisseria gonorrhoeae is the probable cause of these failures. Since penicillin may produce a suppressing, but not curative, action on gonorrhea, careful follow-up studies are important.

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Joseph Dressler supplied technical assistance in this study.

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CLINICAL NOTES

SCREENING FOR DIABETES BY THE GLUCOSE OXIDASE METHOD

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Recently there has been increasing interest in screening programs for diabetes, and several different screening methods have been advocated.[1] The results of screening programs differ considerably, depending on the age, weight, and family history of the group screened; on the type, technique, and standards of screening; on the extent of diagnostic evaluation; and on the diagnostic criteria for diabetes mellitus used in the program.[1a]

Although there is disagreement as to the choice of a screening procedure, certain general principles are acceptable to most authorities.[1c] It is generally recognized that, while the glucose tolerance test would be the ideal procedure, it is too expensive and too complicated for most large-scale programs. The combination of a urine sugar test and a postprandial blood sugar test is considered to be one of the most effective methods, but this has a limited application because of the necessity of obtaining a blood specimen. It is obvious that the urine sugar test is simpler and less expensive than the above procedures. However, heretofore only the copper reduction method has been available. This test is not specific for glucose, giving positive results with fructose, lactose, and other reducing substances.[1c] In addition, this technique tends to detect frank diabetes but to overlook mild or latent cases in which early treatment may be indicated.

Recently, specific enzymatic tests for glucose have become available.[2] These enzymes are flavoproteins which catalyze the aerobic oxidation of glucose to gluconic acid with the production of hydrogen peroxide. The presence of glucose in urine is detected by color changes of reagent-treated paper. The enzyme tests are specific for glucose in amounts as small as from 0.01 to 0.1%. Negative results have been obtained in the presence of lactose, fructose, xylose, mannitol, acetylsalicylic acid, amphetamine, barbiturates, sulfonamides, quaternary ammonium compounds, and hexylresorcinol. In view of the specificity of these tests for glucose, it was considered worthwhile to conduct a detection survey utilizing them in comparison with a copper reduction method.

Materials and Methods

The survey was held during Diabetes Detection Week. A booth was set up in the lobby of the University of Illinois Research and Educational Hospitals, and personnel associated with the professional schools were urged to bring a urine specimen to the booth one hour after a full meal. The specimens were tested for reducing substances by a commercial copper sulfate tablet test (Clinitest) and for glucose by two glucose oxidase tests (Clinistix and Tes-Tape). If the result of any one of the three tests was positive, a glucose tolerance test was done. The "true glucose" method of Somogyi-Nelson[3] was used for determination of the blood glucose level, and the glucose tolerance test was done as follows: a fasting venous blood specimen was obtained, a calculated dose (1 Gm. per kilogram of body weight) of glucose was given orally, and venous blood samples were obtained at intervals

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of one-half, one, and two hours. The criteria used for the diagnosis of diabetes were those of Mosenthal,[4] i. e., a fasting blood glucose level of more than 100 mg. per 100 ml., a one-hour level of more than 150 mg. per 100 ml., and a two-hour level of more than 100 mg. per 100 ml.

Results

In all, 742 urine specimens from as many individuals were examined. In 30 cases, positive results with one or more techniques were obtained. These 30 persons were recalled, and evaluation was done for diabetes mellitus. The data obtained are summarized in table 1. The first 11 patients are diabetics, with the disease previously unknown in 8. Five patients had borderline glucose tolerance findings and are classified as "doubtful normal." This group has been called prediabetic, latent diabetic, hidden diabetic, or possible diabetic, and such patients should be watched for possible future development of diabetes.[5] Six patients had non-glucose-reducing substances in their urine specimens. Two had renal glycosuria. There were six normal persons.

TABLE 1.—*Clinical and Laboratory Data in Evaluation of Positive Findings in Screening Test for Diabetes*

Case	Age, Yr.	Family History of Diabetes	Previous Glycosuria	Weight, Lb.	Clinitest* 2 Drops	Clinitest* 5 Drops	Tes-Tape†	Clinistix†	Glucose Tolerance Fasting	Glucose Tolerance 30-Min.	Glucose Tolerance 60-Min.	Glucose Tolerance 90-Min.	Glucose Tolerance 120-Min.	Comment
1	43	+	+	165	2+	2+	1/2	+	...	...	...	...	...	Known diabetes
2	30	+	+	135	2+	2+	1/2	+	...	...	...	...	...	Known diabetes
3	53	—	+	190	—	1/4	1/10	+	141	...	...	...	...	Known diabetes
4	57	+	—	188	±	1/4	1/10	+	97	160	208	151	85	Diabetes
5	18	+	—	153	—	1/4	1/10	+	96	162	148	88	73	Diabetes
6	24	—	+	160	—	1/4	1/4	+	102	168	180	121	59	Diabetes
7	49	—	—	167	—	—	1/10	+	106	174	238	84	60	Diabetes
8	55	—	+	200	2+	2+	1/2	+	188 101	... 141	... 179	... 123	... 99	Diabetes
9	37	+	—	153	—	1/4	1/10	+	82	123	180	159	93	Diabetes
10	50	—	—	133	—	—	1/10	±	85	213	200	138	68	Diabetes
11	45	—	—	145	1/4	+	1/10	±	100	165	190	144	78	Diabetes
12	23	—	—	145	1 1/2	+	1/2	+	94	142	158	96	80	Doubtful normal
13	45	—	—	179	—	—	1/10	±	91	152	107	68	79	Doubtful normal
14	19	—	—	175	—	—	1/10	+	89	143	157	131	76	Doubtful normal
15	29	—	+	134	—	1/4	1/10	+	90	150	123	64	84	Doubtful normal
16‡	57	—	+	170	3/4	1/2	1/2	+	...	...	...	...	...	Doubtful normal
17	64	—	—	...	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
18	34	—	—	140	—	1/4	—	—	...	...	...	...	...	Lactose
19	54	—	—	122	1/2	1/2	—	—	...	...	...	...	...	Non-glucose-reducing substance
20	32	—	—	118	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
21	30	—	—	135	—	1/4	—	—	...	...	...	...	...	Lactose
22	20	—	—	112	—	1/4	—	—	...	...	...	...	...	Non-glucose-reducing substance
23	26	—	—	120	3/4	1	1/2	+	59 78	71 106 Urine+	75 101	73 83	79 75	Renal glycosuria
24	40	—	—	200	—	—	1/10	±	91	128 Urine+	97 Urine+	56	90	Renal glycosuria
25	28	—	—	150	—	—	1/10	—	92	149	84	81	78	Normal
26	24	—	—	170	—	—	1/10	±	81	139	104	73	82	Normal
27	68	+	—	180	—	1/4	1/10	—	...	...	...	...	...	Normal
28	22	+	—	162	—	—	1/10	±	91 90	122 116	106 108	102 100	111 99	Normal
29	19	—	—	155	—	—	1/10	±	95	135	90	105	97	Normal
30	46	—	—	160	—	—	1/10	±	91 92	130 136	114 153	65 90	62 50	Normal

* Copper sulfate tablet test.
† Glucose oxidase test.
‡ Abnormal glucose tolerance test; details not available (family physician).

A comparison of the results of the tests is shown in table 2. Here it can be seen that diabetes in 2 of the 11 subjects was detected by the glucose oxidase methods but not by the copper sulfate method. Two of the five doubtful normal persons had positive findings in the glucose oxidase tests only. Of the six urine specimens containing non-glucose-reducing substances, positive results were obtained only by the copper sulfate method; none were positive by either of the enzyme methods. One case of renal glycosuria was detected only by the glucose oxidase method. Of the six normal subjects, five showed positive findings in the glucose oxidase method and one in the copper sulfate method.

Thus, of 18 subjects including 11 diabetic persons, 5 doubtful normal persons, and 2 persons with renal glycosuria, negative results were obtained in 5 by the copper sulfate method. Positive results were obtained in all by the glucose oxidase method. Of 12 subjects without diabetes, positive results were obtained by the copper sulfate method in 7 (6 with non-glucose-reducing substances and 1 doubtful normal person). Positive results in the glucose oxidase tests were obtained in five subjects who had normal glucose tolerance findings.

Comment

Screening procedures for diabetes are judged on specificity and sensitivity.[1e] Sensitivity, meaning that a high percentage of persons with the condition should show positive results, was high with the glucose oxidase tests in this survey. In any screening program, it is not possible to know how many subjects actually have diabetes mellitus. Therefore, sensitivity must be estimated by comparing percentage screened who have positive findings in this study with that in other studies. The result of 4% compares favorably with the 86,865 individual examinations collected from several surveys by Wilkerson and co-workers,[1e] in which the average was 2.1%, with a range of 1.3 to 9.0%. In all of these studies a test of blood sugar level was utilized as the screening procedure.

TABLE 2.—*Comparison of Tests with Positive Results in Detection of Diabetes*

	Subjects, No.					
Test	Total	Diabetic	Doubtful Normal	Non-glucose-Reducing Substance	Renal Glycosuria	Normal
Total	30	11	5	6	2	6
All 3 methods	13	9	3	...	1	...
Clinistix* and Tes-Tape*	9	2	2	...	1	4
Clinitest† and Tes-Tape	1	...	...	...	...	1
Clinitest alone	6	...	...	6	...	...
Tes-Tape alone	1	...	...	...	...	1
Clinistix alone	0	...	...	...	...	...

* Glucose oxidase test.
† Copper sulfate tablet test.

Of the total group screened, 1.5% had diabetes. This also compares favorably with respect to sensitivity with the collected average percentage of Wilkerson and associates of 0.5% (range, 0.2-2.0%). Another indication of the relatively high sensitivity of the study is shown by the fact that 36% of those screened with positive results had diabetes, which compares favorably with the average of Wilkerson and associates of 24%, with a range of 22 to 64%.

The criterion of specificity, i. e., that a high proportion of persons not having the condition should show negative findings, is fulfilled at least as well by the enzyme tests as by the copper reduction method. According to the diagnostic evaluation, 12 of the 30 subjects with positive results on screening were probably entirely normal. In this group, seven positive results were obtained only with the conventional copper sulfate method and five only with the glucose oxidase tests.

Thus, the glucose oxidase tests were demonstrated to be satisfactory screening methods for diabetes mellitus. Although sensitivity is higher than with the copper sulfate method, the number of false-positive results is no greater; it is considered that the early detection of diabetes mellitus is enhanced by the use of glucose oxidase tests. Since it has been established that transient glycosuria frequently precedes diabetes,[5b] the high sensitivity of the new methods may be of value in detecting persons with doubtful cases of diabetes who should have periodic evaluation.

Summary

Two glucose oxidase tests for glycosuria were compared with a copper reduction method in screening 742 subjects for diabetes mellitus. Of 30 persons with positive findings on the screening tests, 11 had diabetes. The glucose oxidase tests were more sensitive and more specific for glycosuria than the copper sulfate method. The results are comparable to those obtained in surveys where a test of blood sugar level is utilized as the screening procedure.

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The copper sulfate tablet test (Clinitest) and one of the glucose oxidase tests (Clinistix) used in this study were supplied by Ames Co., Inc., Elkhart, Ind. The other glucose oxidase test (Tes-Tape) was supplied by Eli Lilly and Company, Indianapolis.

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NEW INSTRUMENT FOR BIOPSY OF THE CERVIX AND ENDOCERVIX

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The perfection of cytological techniques in the detection of early carcinoma of the cervix has necessarily required the widespread use of cervical biopsy for confirmation. The frequent small size of the lesions, their clinically inconspicuous appearance, involvement of the endocervix, and the ease with which they may be destroyed, lost, or rendered undiagnosable by the usual techniques of biopsy have indicated the development of new instruments and methods.

When carcinoma is strongly suggested by cytology but the cervix is clinically free of an obvious lesion, the cold cone is recommended to confirm the diagnosis and define its extent and aggressiveness. However, especially in pregnancy, often reports are given of "cells suspicious of malignancy" or "inconclusive findings," their frequency depending on the competence, self discipline, and philosophy of the cytologist. Here, a less rigorous procedure is permitted, avoiding the disadvantages of hospitalization and the risks of hemorrhage and stenosis. Toward this purpose, a new cervical biopsy instrument termed the Cervicotome is presented. It is designed to obtain tissue specimens from the portio vaginalis, the squamocolumnar junction, and the cervical canal (a "pancervical" biopsy).

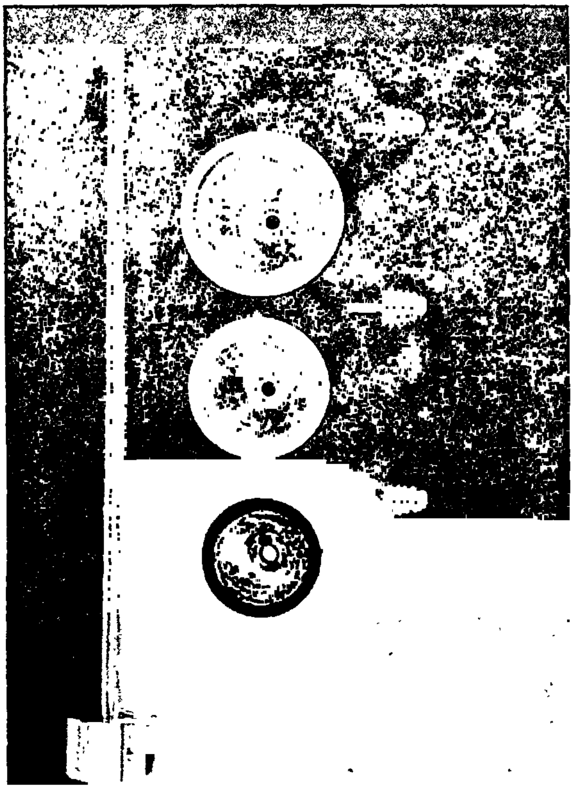

Fig. 1.—Cups, matched blades, and coaxial cutting plug attachments, of several sizes, of biopsy instrument. These are designed to accomodate variations in size of cervix, cervical os, and cervical canal.

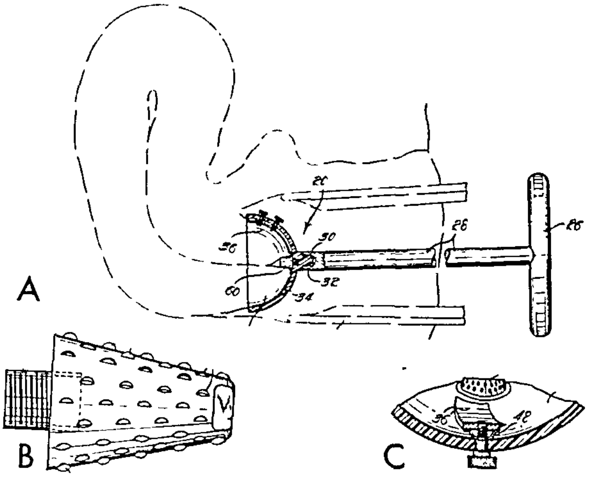

Fig. 2.—*A*, operating position of biopsy instrument, with coaxial cutting plug in cervical canal (60) and cutting blade (36) in contact with cervix. *B*, enlarged drawing of coaxial cutting plug, showing multiple cutting teeth. *C*, detailed drawing of Lucite cup, razor-edged cutting blade (36), and micrometer adjusting screw (48) which determines depth of cut.

This instrument is basically a hemispherical cup attached to an elongate handle. The cup includes an internal curved knife and a coaxial attachment, with multiple serrated cutting edges (fig. 1). The cup and knife are applied over the cervix to remove tissue from part or the entire surface of the cervix, from the external os to a major portion of the portio vaginalis. The concentric cutter will simultaneously obtain small specimens of epithelial and subepithelial tissue from the canal. The cup is made of Lucite to permit the operator to monitor the cutting action.

Operation and Results

With the cervix exposed with a vaginal speculum in place, the Lucite cup is applied to the cervix, with the concentric cutter attachment in the cervical canal (fig. 2). Appropriate pressure is applied to the handle of the instrument as it is rotated in a clockwise direction. Counterpressure may be applied to the fundus with the operator's left hand on the abdomen, at the discretion of the operator. The instrument may be rotated a full 360 degrees where no gross lesions or ulcerations are present on the portio vaginalis.

The instrument may be used in conjunction with Schiller's test and in areas of exophytic growth or gross ulceration. It should be emphasized that the instrument is designed to perform a cutting, rather than a scraping, function. Thus, the physician obtains specimens for definitive histological diagnosis. The specimens obtained from the portio vaginalis and the cervical canal may be examined separately, so that the general location of the lesion will be indicated.

The material obtained is adequate for study, consisting of both squamous epithelial and endocervical tissue and including the junctional zone. The tissue is well preserved, showing less artifact than that obtained by other methods. Necessarily, it is representative of the entire circumference of the cervix, and sufficient lamina propria is obtained to judge infiltration of the stroma.

Summary

A new cervical biopsy instrument, the Cervicotome, is designed to obtain tissue from the portio vaginalis, the squamocolumnar junction, and the cervical canal in one rapid operation. Its use is intended for office practice on ambulant patients, where the cytological diagnosis has been reported doubtful or suspicious, where an infiltrative lesion is probable, or where the patient has refused hospitalization.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for all drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations.

H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN BRONCHIAL ASTHMA

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Bronchial asthma is a distressing and common form of acute, recurrent, or chronic bronchial inflammation and obstructive emphysema, usually of allergic origin. The acute paroxysm of bronchial asthma may last for hours or recur in varying degrees of severity for days. Finally, a state of intractable asthma, during which the episode is continuous and refractory to treatment, may result. In this state the patient presents a picture of marked physiological imbalance. Evidence of hypoxia, cyanosis, dehydration, disturbed psyche, peripheral vascular collapse, and further disturbances may be noted because of changes induced by the widespread use of drug therapy. Death is more commonly due to asphyxia resulting from the plugged and obliterated bronchi and bronchioles and from oversedation; it is also due to the failure of endogenous discharge of adrenal hormones necessary in the defense mechanism against stress, and, in more recent years, particularly to steroid sequelae.

Medical Management

The successful management of the patient with chronic bronchial asthma requires a very careful consideration of the responsible factors in bronchial asthma. Such factors include allergic factors (inhalants, ingestants, contactants, injectants), common colds, paranasal sinus disease, bronchitis (allergic, asthmatic), physical factors (seasonal and climatic influences), psychosomatic factors, and miscellaneous factors (exertion, fatigue, endocrine influence, nonspecific pulmonary irritants, infections).

Every attempt should be made to determine the responsible antigens. If a detailed history is inconclusive as to the cause of a patient's bronchial asthma, then scratch testing and intradermal testing may be resorted to. Removal of the offending allergen (allergic cleanliness) and a trial with specific hyposensitization should be promptly instituted in all cases whenever possible. Further therapy should be directed toward removing the contributory factors. Because search for the responsible agents is

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difficult and often completely unsuccessful, emphasis on the allergic approach to management should not exclude physiological therapy.

Epinephrine.—Epinephrine has been employed in various modifications, concentrations, and routes. Toxic reactions, intolerance, and fastness are more commonly observed with overdosage and repeated parenteral use. Deaths have been reported after intravenous administration. In general, epinephrine given parenterally is limited in its value for the relief of the acute attack. Unfortunately, few physicians or patients limit the dosage to the proper and effective subcutaneous injection of 0.2 to 0.3 cc. of a 1:1,000 dilution of epinephrine hydrochloride. Generally, larger doses at frequent intervals are resorted to, especially when self-administered. The use of the hypodermic needle for self-medication is encouraged too often; the epinephrine-fast state is encountered most commonly in these patients. We have not observed any value from preparations of epinephrine 1:500 in oil.

Most patients in status asthmaticus are epinephrine-fast, and the repeated use of all epinephrine preparations should be avoided until epinephrine sensitivity is restored. We have made a rule of never adding epinephrine to the so-called intravenous cocktail (i. e., intravenous infusion of aminophylline, iodides, dextrose, etc.).

Bronchodilator Aerosols.—Aerosols of sympathomimetic drugs, such as 2.25% racemic epinephrine (Vaponefrin) hydrochloride, isoproterenol (Aludrine, Isuprel) hydrochloride 1:200, a combination of 2.5% racemic epinephrine hydrochloride with 0.5% atropine sulfate (Dylephrin), or a combination of 0.4% isoproterenol sulfate with 2% phenylephrine hydrochloride (Nebu-Prel) have proved to be of great value for the relaxation of bronchospasm. As little as approximately 0.05 to 0.10 cc., nebulized by three to six compressions of a hand bulb, may abort or relieve a mild bronchospastic episode. We have observed clinical and laboratory improvement with administration of these agents.

Recently, epinephrine and isoproterenol have been added to Freons in the form of simple pocket units (Medihaler-Epi and Medihaler-Iso) designed to deliver measured aerosol dosages. The Medihaler-Iso unit is popular with patients and produces improvement in timed vital capacity relationships as tested in those with mild or moderate attacks of bronchial asthma. The class of Freons used to power this has been described as free of toxicity. More recently, a Freon-powered pocket unit has become available with an ingenious reservoir chamber with a self-cleaning, baffling device (Nebu-Halent). This device makes it possible to deliver finer, smaller particle-sized aerosols of bronchodilator agents or other therapeutic aerosols as prescribed by the physician. We were able to determine that in mild paroxysms of bronchial asthma three inhalations with this device, and in moderately severe paroxysms six inhalations, brought effective clinical relief and improvement in timed vital capacity relationships.

More severe bronchospasm may require 0.5 to 1.0 cc. of one of these bronchodilator agents nebulized continuously with oxygen or with the simple Eliot air-pump unit made by the National Cylinder Gas Division of the Chemetron Corp. This treatment generally requires 10 to 15 minutes at a flow rate of four liters per minute.

Aminophylline.—Patients vary in their tolerance to aminophylline. Some become more alert; others become drowsy; many become nauseated and even vomit; and still others complain of palpitation and sweating.

Oral Route: For the prevention of mild but chronic attacks of bronchoconstriction, aminophylline may be given orally, around the clock. The addition of antinausea factors (local and central acting) to aminophylline has made possible the oral administration of larger, effective doses, with or without the addition of ephedrine, iodides, or a barbiturate. A combined preparation containing 300 mg. of aminophylline, 150 mg. of aluminum hydroxide, and 30 mg. of ethyl aminobenzoate (Cardalin), or a preparation containing 200 or 250 mg. of aminophylline, with 15 mg. of ephedrine hydrochloride or 25 mg. of phenobarbital and 15 or 30 mg. of pentobarbital sodium, 150 mg. of aluminum hydroxide, and 15 mg. of ethyl aminobenzoate (Dainite) is most helpful when the dose is carefully tailored for the individual patient's needs and tolerances.

Rectal Route: For more persistent attacks, aminophylline should be administered rectally in doses of 300 to 600 mg. in 15 cc. of tap water every 8 or 12 hours. For children, the dose may be reduced to 60 to 200 mg. The available suppositories are not of equal value.

Intravenous Route: Aminophylline should be given intravenously for severe paroxysms of coughing or wheezing not relieved by epinephrine or bronchodilator aerosols or by aminophylline given rectally. For an attack which has persisted for less than 12 hours, 250 mg. in 10 cc. of water for injection usually brings prompt relief. For a more protracted attack, the dose should be 500 mg. in 200 cc. of water for slow intravenous injection. These infusions may be repeated at intervals of 8 or 12 hours. Syncope and peripheral vascular collapse may be observed if the rate of injection is too rapid (1 cc. per minute is suggested).

For a severe acute attack of bronchial asthma occurring at home, which has failed to respond to self-administered bronchodilator aerosols, epinephrine, sedation, or oral forms of aminophylline, the following routine may be most helpful: 1. A dose of 500 mg. of aminophylline in 20 cc. of solution may be given intravenously. 2. If no lasting relief is observed in half an hour, 0.2 cc. of epinephrine gel (Sus-Phrine) may be given subcutaneously. 3. If no lasting relief is observed in 15 minutes, 75 mg. of meperidine (Demerol) hydrochloride may be given subcutaneously.

If the patient has not previously used adrenergic agents, the order should be reversed to epinephrine gel, aminophylline, and meperidine hydrochloride. The attending physician should move quietly, yet act quickly, with assurance and empathy. The patient who does not respond satisfactorily in one hour's time would benefit most by proper hospitalization.

Continuous Infusion Technique: If intravenous injections of aminophylline become necessary one or more times daily for as long as a week, the continuous infusion technique should be employed. The patient should be hospitalized. A solution is made containing 500 mg. of aminophylline in each liter of 5% dextrose in water. Three liters should be given in 24 hours, with a flow rate of 30 drops per minute. If improvement follows after one or two days of such therapy, the infusions then may be given intermittently, e. g., from 9 a. m. to 9 p. m. daily, reducing the total to 1,500 cc. For the very sick patient, it may be necessary to continue these infusions for as long as 10 days. During convalescence, aminophylline should be given rectally instead of intravenously.

By means of pulmonary function studies, we have demonstrated the presence of latent bronchoconstriction in the patient who has completely recovered. Hence, in these patients, orally given aminophylline in combination with aluminum hydroxide and ethyl aminobenzoate should replace the rectally given aminophylline used during convalescence.

Intermittent Positive Pressure Breathing Therapy.—The use of pressure breathing is based on the creation of a pressure gradient from the mouth down to the pleural space. In the intermittent types, the gas mixture is supplied in the inspiratory cycle, usually through a face mask. There are several effective types of mask apparatus units which supply intermittent positive pressure breathing in inspiration. We have found the Bennett-type cycling valve and the new, extremely sensitive Mark 7 unit most satisfactory for administering positive pressure breathing, especially when combined with inspiratory bronchodilator aerosols. The patient completely controls the cycling of the valve by his own respiratory rhythm. An active inflation of the lungs occurs during inspiration under positive pressure from the cycling valve. The rapid release of pressure at the start of expiration is followed by a high velocity expiratory gas flow. This, combined with the release of bronchoconstriction which follows the simultaneous inhalation of bronchodilator aerosols, promotes better bronchial drainage. We employ pressures of 10 to 15 cm. H_2O with mixtures of air and oxygen. In general, this form of therapy should be reserved for the patient with chronic recurrent attacks who has some degree of complicating ventilatory insufficiency responsible for his disability. It is most useful in reeducation of diaphragmatic breathing and prevention of carbon dioxide retention. We have recently been able to demonstrate actual reduction in mechanical resistance and increase in pulmonary compliance, with resultant lowering of the work of breathing in these patients employing the Mark 7 unit.

In the presence of bronchial infection, bronchiectasis, or tenacious purulent secretions, the use of enzyme aerosols to attack the pus, such as pancreatic dornase (Dornavac), is indicated. It has proved to be efficacious in clearing bronchial infection of a chronic nature. Pancreatic dornase, dissolved in 0.5 or 1 cc. of the bronchodilator aerosol, is administered by aerosol in doses of 50,000 to 100,000 units, one to three times daily for five to seven days, with the continuous aerosol technique or with intermittent positive pressure breathing. It is used in addition to, not instead of, antimicrobial therapy.

Therapeutic Gases.—Oxygen Therapy: If there is hypoxia and cyanosis, the patient should be given oxygen. His physical and personal requirements, as well as the concentration of oxygen desired, should be considered in selecting the type of equipment to be used. Unfortunately, most patients in status asthmaticus tolerate poorly the tight-fitting rubber face masks which are necessary when concentrations of oxygen above 60% are indicated. The simple Eliot plastic face tent supplies average concentrations of 50% oxygen in the inspired air, with oxygen flow rates of six liters per minute. The patients do not complain of claustrophobia or a sense of suffocation.

In general, there has been an overemphasis on the danger of inducing the carbon dioxide intoxication syndrome and respiratory acidosis by the sudden administration of high concentrations of oxygen in patients with classic intractable bronchial asthma. This danger, however, is always present in patients with chronic hypoxia secondary to chronic pulmonary emphysema or chronic pulmonary heart disease, particularly if respiratory depressing drugs are administered before, or along with, the high concentration of oxygen. In these patients the plastic nasal cannula-humidification technique is best employed. Initial low concentrations with flow rates of one liter per minute should be used. The flow rates may be cautiously increased by daily increments to six liters per minute, and subsequently the therapy may be maintained more simply and safely with the Eliot plastic face tent.

Helium-Oxygen Positive Pressure Breathing: If obstructive phenomena predominate, mixtures of 75% helium and 25% oxygen are more beneficial than oxygen alone. Subjective relief of dyspnea and wheezing may be observed frequently after positive pressure breathing of helium-oxygen mixtures. The gas mixture may be administered through the metered mask apparatus (made by the National Cylinder Gas Division of the Chemetron Corp. or by the Oxygen Equipment Manufacturing Corporation) which supplies an expiratory positive pressure when the exhaled air passes through constricted orifices. This method may be tiring, and the patient should be treated for periods of one-half to one hour four times daily. Rebreathing from the collecting bag may be permitted as an economy measure (helium saving). The intermittent positive pressure breathing unit may be employed; it is most efficacious and less tiring for the patient but more costly.

Bronchial Evacuation ("Catharsis").—The bronchitic cough is one of the most troublesome manifestations and may actually serve as the trigger mechanism for more extensive bronchiolar spasm. The therapeutic mechanisms for bronchial evacuation consist mainly in the use of (1) expectorants, (2) iodides, (3) ipecac, (4) positional drainage, and (5) bronchoscopy.

Expectorants: The expectorant drugs may prove quite helpful when properly used. A patient with an effective productive cough should not be oversedated, or the mucus in the bronchioles may become tenacious and inspissated, largely from dehydration and long retention. If the mucus is permitted to become impacted, the cough may become ineffective, and a state of "tussive insufficiency" will develop. One of the antihistamine preparations, a combination of diphenhydramine hydrochloride and aminophylline (Hydryllin) may be of value, particularly in patients with associated vasomotor rhinitis. Among the more ideal expectorants are the iodides, ipecac, and aerosols of water or detergents such as superinone (Alevaire) and Tergitol 08.

Iodides: Iodides are excellent bronchial evacuants. In the very sick patient, 1 to 2 Gm. of sodium iodide may be added to each liter of infusion fluid and administered for several days. When effective productive coughing occurs, the iodides may then be given orally again. Their action results in dilution and liquefaction of the retained secretions. Iodides are more efficacious when the patient is well hydrated. A disagreeable metallic, bitter taste is commonly experienced. The usual precautions in the use of iodides should be observed; namely, close watch for evidence of a variety of rashes and swelling, conjunctivitis, coryza, bronchorrhea, thyroiditis, and adenopathy. Administration should proceed cautiously. The initial dose should be 0.2 cc. of the saturated solution of potassium iodide after each meal and at bedtime. This may be increased by 0.1 cc. per dose each day until a maximum dose of 1.3 cc. is reached. The dose should then be abruptly reduced to 0.2 cc. and the same gradual increase of dosage repeated; this may prevent the development of intolerance. For patients in whom gastric irritation develops from a saturated solution of potassium iodide, enteric-coated tablets are available in 500 mg. and 1 Gm. sizes.

Ipecac: Ipecac acts by substituting effective retching in the place of ineffective coughing. Syrup of ipecac may be administered in doses of two or three teaspoonfuls followed by a cup of lukewarm boiled water. This dose may be repeated several days later, if indicated. It is always worth a trial before bronchoscopy is attempted.

Positional Drainage: Although of little benefit to those with useless cough, positional drainage may be of considerable value to the patient with accumulated secretions that are easily raised. The procedure is generally most efficacious in the management of associated bronchiectasis. It is more effective when carried out after bronchodilator therapy.

Bronchoscopy: One of the most common and important causes of death in asthma is obstruction of the larger and smaller air passages by inspissation of tenacious secretions. At times, spectacular improvement may follow bronchoscopic aspirations, even in a moribund patient. Because of the danger of serious reactions to the use of tetracaine hydrochloride or cocaine sprays and instillations for local anesthesia in asthmatic subjects, we generally prefer deep surgical anesthesia with ether. Intensive bronchoscopic aspiration is followed by marked subjective and objective improvement. It may prevent atelectatic complications, prove lifesaving, and be followed by a long period of remission.

Antitussive Measures.—The most effective antitussive measures center about the prevention of various trigger mechanisms responsible for the coughing paroxysms. Laughter, shouting, talking, crying, inhalation of tobacco smoke, dusts, fumes, fogs, and smogs, sudden changes in temperature and humidity, and exertion are among the leading causes in precipitating troublesome coughing paroxysms, which frequently induce bronchospastic crises, expiratory ball valving, and actual alveolar disintegration. The patient should always be on the alert for these causes, and the sooner he learns his tolerance to these factors the more successful the "cure."

In a recent study in our laboratory we found that benzonatate (Tessalon) was a most helpful agent in the management of pharyngitis and tracheobronchitis. Administered as an aerosol or syrup sipped slowly, this preparation has a pleasing surface-anesthetic effect which, though short-lived, is free of the side-reactions observed with the "caine" preparations. When given orally (in the form of perles), there is suggestive evidence that the antitussive effect occurs by action at the pulmonary parenchymal proprioceptor centers. For more sustained effects in the patient with intractable coughing paroxysms during the daytime, intensive therapy with noscapine (Nectadon), 30 to 60 mg. given orally at graded intervals, has proved quite beneficial. We have not observed respiratory depression, significant drowsiness, or constipation with its repeated use. At bedtime, 15 to 30 mg. of dihydrocodeinone bitartrate has been most beneficial in suppressing the severe nocturnal coughing paroxysms.

Sedation.—Anxiety, fear, insecurity, restlessness, nervousness, insomnia, and mood and personality deviations are commonly encountered in patients with chronic recurrent attacks. These symptoms and a frank "alert state" may be accentuated by the very medications that these patients require, namely, aminophylline, adrenergic compounds, and the corticosteroids.

Heavy sedation should be avoided and only agents with a wide margin of safety used. Sodium bromide or chloral hydrate are helpful for the patient with mild, chronic recurrent attacks. When an attack has persisted for more than several hours, sedation should be given in addition to epinephrine and aminophylline given intravenously.

Meperidine hydrochloride, used in proper dosage, is a useful and safe drug in the treatment of the patient in an acute asthmatic attack or in status asthmaticus when the usual methods of treatment have failed or when fastness to epinephrine or aminophylline has developed. It has a far wider range of safety than morphine. The use of meperidine for a total of two to five days, administered at intervals of six to eight hours orally or parenterally in doses of 50 to 100 mg., has not caused addiction in our patients, even when this course was repeated at intervals of several weeks. However, we do not recommend its routine use in any of these patients. Meperidine can, of course, depress respiration if given in too large a dose or if repeated too frequently in patients with chronic bronchial asthma and associated emphysema.

If meperidine is contraindicated or not well tolerated, a retention enema of paraldehyde (20 to 30 cc.) or ether (60 to 70 cc.) may be administered at intervals of six or eight hours. These have proved of particular value in seriously ill asthmatic patients. Unfortunately, they are often irritating and difficult to retain.

Chlorpromazine (Thorazine), prochlorperazine (Compazine), and meprobamate (Equanil, Meprospan, Miltown) or similar "tranquilizers" may be of considerable clinical value in allaying the anxieties of seriously ill patients. In the hospitalized patient, 50 mg. of chlorpromazine hydrochloride may be administered intramuscularly upon admission and at eight-hour intervals for two to four days. Many patients with marked mood swings, anxiety, and compulsive behavior patterns receive considerable benefit from carefully selected, relatively nontoxic "tranquilizers" when administered over periods of many months. The pepped-up reactions and mood swings noted secondary to corticosteroid therapy have also been allayed in many patients with the simple addition of meprobamate plus prednisolone (Meprolone).

Management of Infections.—Evidence of respiratory tract infection is present in most patients with intractable bronchial asthma. Study of the sputum usually reveals polymorphonuclear leukocytes, bacteria, or pus in these patients. The leukocyte count, polymorphonuclear counts, and sedimentation rate may also be elevated. In general, the choice of the antimicrobial agent depends upon the predominating organisms, their drug susceptibility, and the patient's tolerance for the drug itself. Perceptive clinical judgment, tempered by practical bacteriological observations, is necessary in deciding what drugs or combination of drugs and dosages should be employed in an attempt to suppress the total infection. Complete eradication occurs rarely.

Although the clinical activity of penicillin is entirely confined to infections caused by gram-positive micro-organisms, it is the most useful agent in these patients. Unfortunately, the high incidence of local or generalized allergic reactions to penicillin aerosol in these patients limits this technique, which is otherwise most useful for the management of chronic bronchial infections. Penicillin is of particular value for hemolytic streptococci, since one does not usually encounter resistance. Unfortunately, an increasing number of strains of hemolytic staphylococci are penicillin-resistant. In these instances, erythromycin (Ilotycin), novobiocin (Albamycin, Cathomycin), kanamycin (Kantrex) sulfate, or chloramphenicol (Chloromycetin) should be administered. Because of the finding of mixed gram-positive and gram-negative organisms in most of our hospitalized patients seriously ill with intractable bronchial asthma and respiratory tract infections, we have administered combinations of 300,000 units of procaine penicillin G and 500 mg. of streptomycin sulfate every 12 hours. These combinations should be employed only for three to seven days because of the development of resistance to streptomycin in numerous instances. The incidence of severe reactions to penicillin given parenterally in patients with chronic bronchial asthma is higher than in the general hospital population, and a careful history of previous experiences with this drug should be elicited.

As an alternative or as a primary choice, one of the broad-spectrum antimicrobial agents—oxytetracycline (Terramycin), chlortetracycline (Aureomycin), tetracycline (Achromycin, Panmycin, Polycycline, Tetracyn), or chloramphenicol—may be used. In seriously ill patients, dosages of 250 mg., administered at six-hour intervals during the meal or with a glass of milk, may be employed for several days. The dosages should be tapered downward as soon as possible. Evidence of proctitis, Monilia invaders, granulocytopenia (with use of chloramphenicol), complicating Proteus vulgaris organisms, pseudomonas infections, and idiosyncrasy should always be looked for. The addition of nystatin (Mycostatin) when fungi appear in the sputum is advisable.

Confronted with the problem of an overwhelming bilateral pneumonia in a patient with intractable bronchial asthma which is not responsive to a host of antimicrobial agents, the physician is justified in adding corticotropin (Acth, Acthar, Corticotropin) or soluble hydrocortisone sodium succinate (Solu-Cortef).

Prophylactic antimicrobial therapy is of considerable value in debilitated patients with intractable bronchitis and asthma who are subject to recurrent respiratory tract infections during the winter months. In general, we employ orally one of the following antibiotics in the stated dosages: 500 mg. of sulfadiazine, 100,000 units of penicillin, or 100 mg. of tetracycline, given every 12 hours. These doses occasionally require slight revision.

It should always be kept in mind that to suppress or eradicate bronchial infection it is not sufficient to convert a purulent sputum to a mucoid one. The sputum must be adequately evacuated by employing the aforementioned principles of bronchial evacuation, with the use of positional drainage, expectorants, bronchodilator aerosols, pressure breathing therapy, and bronchoscopy.

An irreparable sinobronchitic syndrome often follows in the wake of chronic paranasal sinus disease. Free drainage of the paranasal sinuses and elimination of infection should be attempted. Allergy appears to be the dominant factor in most patients. The topical use of the "safer" vasoconstrictor drugs, such as phenylephrine hydrochloride in combination with an antihistaminic, corticosteroid, and antibiotic agent, is of considerable aid in maintaining nasal patency and limiting infection. With evidence of frank purulent infection, 100,000 units of potassium or sodium penicillin G may be added to 1 cc. of 1% phenylephrine hydrochloride and administered with the Eliot air pump unit employing nebulizer and nasal tips. Treatments can be given at intervals of four to six hours for days or weeks, as indicated and tolerated.

Remissive Measures.—The use of adrenal steroid therapy should represent but a single phase, albeit important, in the total therapeutic program. Although these hormones frequently have a striking ameliorative, anti-inflammatory, and antiallergic clinical effect (antiphlogistic), they seem only to arrest the disease and usually do not suppress it. They should be employed for restricted and considered use when all other conventional methods of therapy have proved ineffective in securing a remission. Unfortunately, in the management of the patient with chronic bronchial asthma, the physician pushing steroid therapy may find himself like the man holding the tiger's tail because of the problems attendant to withdrawal therapy.

Changes During and After Hormone Therapy: Accumulation of eight years' clinical experience and extensive laboratory studies with these hormones have resulted in recognition of the many side-effects and toxic reactions as well as an appreciation of the precautions and contraindications to be observed. The undesirable effects that may follow the clinical use of hormones may be classified generally into two groups, those caused by overdosage and those caused by withdrawal of the hormone. Since successful steroid therapy depends upon a state of hormone overdosage, it is unavoidable that effective hormone therapy will be associated with an exaggeration of the patient's normal physiological actions. Any of the symptoms and finally the full-blown picture of adrenocortical hyperfunction (Cushing's syndrome) may develop. In particular, diabetes mellitus, gastrointestinal hemorrhage, hypertension, osteoporosis, and growth arrest in children should be closely watched for.

Symptoms of hormone withdrawal are the result of a state of adrenal-insufficiency created by hormonal suppression of adrenocortical function. The symptoms may be mild or severe, depending upon the dosages employed, duration of therapy, and rate of withdrawal of the hormone. This state of relative adrenal insufficiency may resemble the course of adrenal cortical hypofunction (Addison's disease). Any additional stress in the form of trauma, shock, surgery, or severe infection during this state of insufficiency may prove disastrous to the patient.

On decreasing the dose during withdrawal of the hormones, aches and pains, lassitude, and a wide spectrum of personality changes may occur. These symptoms usually clear up when the dose is increased but may recur when another attempt is made to decrease the dose. A delicate balance must be found with each patient.

The wide varieties of changes noted during and subsequent to steroid therapy are listed as follows. The less serious changes include facial mooning, acne, petechiae, purpura, edema, hirsutism, skin pigmentation, increased appetite, insomnia, headaches, aches, pains, weakness, lassitude, euphoria to mild depression, mental and physical hyperactivity, hypertension, tachycardia, glycosuria, hyperglycemia, aggravation of existing diabetes, depressed thyroid function, thrombophlebitis, and sensitivity reactions to corticotropin given intramuscularly, such as skin rashes, pruritus, urticaria, occasional wheezing, and angioneurotic edema. The more serious changes include potassium deficiency, muscular weakness, negative nitrogen balance, osteoporosis and fractures, especially in women after menopause and in immobilized patients, masked infections (bacterial, viral, and fungal), spread of existing infections, serious spread of nonpathogenic inhabitants of the gastrointestinal and respiratory tracts, mental confusion to severe psychotic manifestations, convulsions, exacerbation of quiescent ulcers, gastrointestinal hemorrhage and perforation, activation and spread of unsuspected or inactive tuberculosis, sensitivity reaction (anaphylactic shock), periarteritis, and postoperative adrenal insufficiency. The most serious or fatal changes include the withdrawal syndrome, "adrenocortical storm," poor tolerance to trauma, shock, and infections, and active atrophy of adrenal cortices.

Therapeutic Precautions: Among the therapeutic precautions to be followed are restriction of sodium chloride in the diet to 750 mg. daily, with corticotropin, cortisone (Cortisone, Cortogen, Cortone) acetate and hydrocortisone (Cortef, Cortril, Hycortole, Hydrocortone) therapy. The newer corticoid analogues do not usually require this strict restriction. The occasional use of chlorothiazide (Diuril) may be helpful when indicated by the presence of hypertension and/or the excessive weight gain from fluid and salt retention. Potassium may be routinely administered in the form of a tableted mixture containing 500 mg. of ammonium chloride and 500 mg. of potassium chloride (Pot-Amide), 8 tablets daily. Supplemental potassium in the form of orange or cranberry juice (8 to 12 oz. daily) is preferred by many patients. The supplementary ammonium chloride in the Pot-Amide preparation acts as a mild diuretic agent and is followed by excretion of sodium and water. Potassium replacement is best carried out when the salt-retaining type of steroids is employed. This is of particular value in patients with moon-face, fluid and salt retention, and weight gain syndrome. In the presence of infection or suspected infection, the concomitant use of an antimicrobial is advisable. In general, the patient should receive a high-protein diet to offset the tendency toward negative nitrogen balance. For patients with a tendency toward gastric hyperacidity, it is advisable to prescribe antacids and belladonna alkaloids during hormone therapy. Periodic guaiac tests of finger specimens of stool are advisable in these patients and in others suspected of having gastrointestinal ulceration. When in doubt, a series of x-rays should be taken as a control measure. The use of androgens and/or estrogens is perhaps indicated when the patient receiving hormone therapy has evidence of osteoporosis, noted more usually in patients over 50 years of age who are on long-term therapy. Patients should receive adequate supplemental doses of corticosteroids in case of surgery, severe trauma, or other forms of major stress. To minimize adrenal suppression and atrophy in patients receiving long-term therapy with the corticoids, corticotropin gel may be administered periodically, and particularly when corticoid withdrawal is started.

Hormones.—Hormonal therapy should not be used until all of the other measures which may be indicated have been adequately employed. Finally, hormonal therapy is best employed in conjunction with the foregoing measures to secure a more effective and lasting remission, with the lowest possible dosage schedule and freedom from side-reactions. In patients with severe seasonal (pollen) asthma, short-term therapy should be administered when the patient has failed to respond within a week to intensive antihistaminic and bronchodilator therapy started at the very outset of symptoms.

Oral Route: The following corticosteroids have been used orally in order of their development: cortisone, hydrocortisone, prednisone (Deltasone, Deltra, Meticorten), prednisolone (Delta Cortef, Hydeltra, Meticortelone), methylprednisolone (Medrol), triamcinolone (Aristocort, Kenacort), and more recently, dexamethasone (Decadron, Deronil). In general, it has been our custom to consistently employ lower initial therapeutic and maintenance dosages and to withdraw the drug with smaller reductions and over a longer period of time than reported by other investigators. This is possible when intensive supplemental, physiologically directed therapy is carried out simultaneously. It is our belief that fewer significant side-reactions will then be observed. Nevertheless, a continuous high index of suspicion of the hazards previously listed must be maintained at all times. This applies to all corticoid analogues, regardless of their purported safety features.

We have observed considerable variations in individual responses to the steroids. On occasion, a patient not responsive to prednisolone has shown dramatic improvement with cortisone or hydrocortisone. Similar observations may be noted with the newer prednisolone analogues triamcinolone and dexamethasone. The physician should be prepared to change preparations from time to time. The advantages of less profound alteration in potassium depletion and sodium retention, in the face of adequate anti-inflammatory properties, and the ability to select the agent best suited for the individual patient's appetite needs have given these newer corticoid analogues a more desirable status for general use than the parent compounds, cortisone and hydrocortisone.

During the seasonal (pollen) bouts of bronchial asthma, steroid therapy should be employed on a short-term basis only when the more conservative physiological measures have failed. Therapy over the shortest period of time commensurate with the patient's pollen season is usually adequate. The patient with tree, grass, and ragweed pollen asthma may not require therapy during the entire period from spring to Labor Day. Individual variations in sensitivity to different pollens may be elicited in careful history taking of previous years. The patient with ragweed pollen asthma is particularly grateful.

For the patient with chronic, intractable bronchial asthma, when vigorous therapy has failed, long-term steroid therapy becomes necessary. The physician does well to be "reluctantly forced into therapy" rather than to start it at once. He should not be motivated by the desire to show the patient, his family, and friends a brilliant therapeutic result by first starting steroid therapy.

During the past three years we have observed the effects of prednisolone in more than 400 adult patients with various types of chronic bronchial asthma and associated allergies. The dosage schedule most commonly followed was 5 mg. four times daily for the first three days, 5 mg. three times daily for four days, 5 mg. twice daily for seven days, and 5 mg. or less daily thereafter. Approximately 10% of the patients were able to remain on maintenance doses of 2.5 mg. Another 10% required slightly higher revisions initially and for maintenance. The majority of the patients were maintained on 5 mg. daily. During periods of unexplained stress or infections, the patients were permitted to return to their initial starting schedule, followed by the same gradual reduction. The reduction in dosage for withdrawal from long-term therapy is presently advised at 1 mg. per month. The drug may ultimately be spaced at intervals of two or three days during withdrawal. Preparation for surgical procedures is accomplished by returning to the full initial schedule two days before surgery. At times, supplemental hydrocortisone sodium succinate therapy given intravenously on the day of and after surgery is advisable.

With the use of prednisolone-meprobamate, we have not observed any over-all reduction in the basic dosage requirements. However, many patients with steroid-alert manifestations and patients during the pollen season appear to prefer this combination. It was considered best to maintain patients, with a past history of gastrointestinal bleeding, on buffered prednisolone (Co-Hydeltra). Supplemental antacid therapy is often advisable.

We recently reported on our observations in 44 patients with chronic bronchial asthma and allied disorders who were treated with triamcinolone. An additional 32 patients with chronic bronchial asthma have been studied since this report. There appeared to be a greater weight loss in this series than in the series who were given prednisolone. The over-all results were good; facial mooning and weight gain in some patients, but no serious sequelae, were observed. We have not observed any anorexia, weakness, or clinical evidence of excessive nitrogen or potassium loss in our patients with chronic bronchial asthma. The dosage requirements were on the order of 4 mg. of triamcinolone to 5 mg. of prednisolone (4:5). The schedules previously described for prednisolone were followed.

At the present time, we have under observation 52 patients with intractable bronchial asthma being treated with dexamethasone. This is an unusually interesting new steroid agent; more than one-half of the patients have noted tremendous increase in appetite and consistent weight gain. The weight gain has been influenced but little with supplemental chlorothiazide. However, there appears to be a greater incidence of bleeding from the gastrointestinal tract thus far in our observations. Two patients developed bleeding; one had no history of peptic ulcer, whereas the other gave a history of duodenal ulcer. Dexamethasone appears better suited for the debilitated patient in whom weight gain is important. The dosage of this agent required for suppression of asthma is in the ratio of 1:3, as compared with that of triamcinolone.

Intravenous Route: The intravenous route is more efficacious for the hospitalized patient in serious status asthmaticus. The patient is started on a continuous infusion of 5% dextrose injection, 30 drops per minute flow, thus ensuring approximately three liters per 24 hours. Aminophylline, 250 to 500 mg., is added to each liter, depending upon the patient's responses and tolerance. For the patient who has not received steroid therapy recently, 10 mg. of corticotropin is added to each liter, and a total dose of 30 mg. per 24 hours is given for one to three days. Those who have been on corticosteroids should receive hydrocortisone or hydrocortisone sodium succinate given intravenously. The quantitative eosinophils, which are consistently elevated at the outset, are usually low or absent by the second day of this program. With improvement in the patient, the corticotropin is administered only in the first liter of fluid daily for several more days. In the most severe cases, the infusion of dextrose and aminophylline is continued for an additional one or more days. With intravenous therapy the immediate results are generally more striking. However, the physiological hazards, particularly disturbances in psyche, potassium imbalance, and facial mooning, may be more pronounced.

Attempts should be made to maintain the remissive state with the use of aminophylline solution given rectally or oral preparations of aminophylline and bronchodilator sprays, given as needed. During treatment and after remission, many patients note that they can "do more with considerably less" of their therapeutic armamentarium.

Surgical Management

The proper management of the patient with chronic recurring bronchial asthma may tax the character and ingenuity of the physician. The therapeutic problem may be made even more difficult by the family and the disturbed emotional make-up of the patient. The physician should acquire a proper attitude of empathy rather than overt sympathy, and he should strive to firmly adjust the patient's personality to his disease. A mutuality of confidence must be established. Every severe asthmatic episode should be carefully considered apart from previous seizures. The "whims and cure-alls" of his patient and family should not be curtly dismissed but discussed rationally.

Unfortunately, too often, as with many chronic diseases, the hope of "surgical cures" is brought up. Benefit has been described after a wide variety of surgical procedures, and, indeed, specificity has been "suggested" for these measures. Notwithstanding the great technical skill of the modern thoracic surgical team, there appears but little enthusiasm for the operative procedures designed for the purpose of influencing the neurogenic control of the bronchioles and chemical secretions. Unfortunately, observations made in the laboratory on cats and dogs cannot be translated accurately into changes to be observed in humans with chronic bronchial asthma. Occasionally, brilliant temporary results have been reported after procedures attacking the sympathetic or parasympathetic (vagal) or both systems. These procedures have varied from the simpler procedures designed to block vagal influences, such as procaine injection to the vagal fibers in the mastoid region and procaine or alcohol block of the sympathetic stellate ganglions and the upper four thoracic ganglions, through a variety of unilateral and bilateral cervicothoracic sympatholytic or parasympatholytic designed resections. Finally, bilateral resection (two stages) of the posterior pulmonary plexus as well as resection of cervicothoracic sympathetic and complete pulmonary plexectomies have been performed. No unanimity of opinion as to the ideal surgical procedure for these hapless patients can be found. In fact, most of the early enthusiastic surgical investigators have stopped their search for surgical surcease. Many patients improve temporarily after these procedures. Long periods of rest in the hospital and intensive medical care may well explain this. The physiological and financial stress of major surgery, the attendant pain and discomfort, the complications of pneumothorax with ganglion surgery, trauma to bronchi and blood supply, with intrathoracic procedures and the discomfort of residual, unilateral, or bilateral Horner's syndrome and skin temperature changes noted after sympathetic surgery (the patient "looking and acting like a sad St. Bernard Dog") are quite disconcerting to say the least.

There is still another surgical procedure which has found some favor among thoracic surgeons. Beneficial results have been described in patients in whom excision of "trigger areas" of pulmonary destruction (bronchiectasis) or excision of areas of large emphysematous bullae was carried out. Excisional surgery, along with some type of interruption of the upper sympathetic or parasympathetic vagal chain below the level of the recurrent laryngeal nerve, is usually advocated by these surgeons. Definite bronchiectatic disease (saccular), which is unequivocally demonstrable (after maximal bronchodilation) by radiography and bronchography and which has served as a nidus for recurring pneumonitis, chronic suppurative disease, pulmonary hemorrhage, or progressive debility, should be dealt with as bronchiectasis per se and not as a possible "trigger mechanism" for chronic bronchial asthma. The indications for resectional surgery in these patients are clear-cut and uniformly accepted, and the curative results from the effects of the bronchiectasis are excellent. However, the course of the associated chronic bronchial asthma is usually not affected for long. The segmental bronchial areas, suggesting cylindrical bronchiectasis by radiography or bronchography, should not be resected unless the well-defined criteria referred to previously for resection of a proved saccular bronchiectatic area are present. After resection, lasting improvement should not be expected in the associated chronic bronchial asthma.

Similar criteria should be applied to the patient with chronic bronchial asthma, secondary chronic pulmonary emphysema, and large bullae (seldom seen in this order of relationship). Demonstration of a progressive space-occupying lesion, which is encroaching on functioning lung, an expiratory check-value mechanism, and repeated bronchopulmonary infections with laboratory evidence of ventilatory insufficiency despite adequate therapy, is an indication for surgical intervention in patients with large bullae associated with chronic pulmonary emphysema and secondary bronchospastic crises. The choice of plication, excisional procedure, or another type of tailoring operation should be individualized.

The author has a dim view of the present status of the aforementioned thoracic surgical procedures for the cure or amelioration of chronic bronchial asthma. After surgery these patients generally continue to require long-term intensive medical therapy. Fortunately, physical rehabilitation and the use of adrenal steroid therapy, particularly with the newer corticoid analogues with potentially less mineralocorticoid reactions, intensive bronchodilation, and antibiotic therapy, have made their care more pleasant. Nevertheless, more adequate management of this large group of "pulmonary cripples" continues to remain a challenge to the family physician and the specialist. Unfortunately, these patients all too frequently require an "economic prescription."

The dexamethasone used in this study was supplied as Decadron by Dr. Elmer Alpert of Merck, Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., Rahway, N. J.

COUNCIL ON INDUSTRIAL HEALTH

THE LEGAL SCOPE OF INDUSTRIAL NURSING PRACTICE

This report has been prepared by the Committee on Industrial Nursing of the Council on Industrial Health, American Medical Association, in collaboration with the Association's Legal Division.

B. Dixon Holland, M.D., *Secretary,*
Council on Industrial Health

The purpose of this report is to discuss the legal scope of the practice of industrial nursing and the functions which a professional industrial nurse may legally perform. The intensification of the educational program of nursing, the increased dependence of the physician on the skills and discretion of the nurse, and the ability of the nurse to meet the challenge of an ever-rising standard of patient care have motivated the nursing profession to define and seek recognition for those professional functions which the nurse performs independently. This is especially true of the industrial nurse who often works without immediate medical supervision.

The Practice of Nursing

Nursing and medical practice are interrelated and frequently indistinguishable from each other. The same act may be clearly the practice of medicine when performed by a physician and likewise a practice of nursing, depending on the circumstances, when performed by a nurse.

There are, of course, limitations on the functions which the nurse may perform, whether independently or under the supervision of a physician, and there are likewise limitations on the functions which may be legally assigned by a physician to a nurse. These will be discussed in this report.

The statutes of the various states which define professional nursing are too nebulous to provide a usable guide in determining the functions in which a nurse may legally engage. Essentially the statutes define professional nursing as involving the carrying out of treatment prescribed by a licensed physician and the application of nursing skills. Obviously, such definitions do not identify the particular functions in which a professional nurse may engage.

Probably the lawmakers should be commended for their foresight rather than criticized for ambiguity. A half-century ago when the first nursing practice acts were adopted the principle function of the nurse was to aid the physician by performing tasks under his direction. The functions of nursing are constantly expanding, and precisely drawn statutory definitions of the functions of nursing could not be kept up to date with changes in professional practices. However, the growing body of judicial decisions reflects the development of the profession of nursing and its expanding responsibilities in the wake of medical progress. The identification of particular functions as nursing functions and the standards of competence required of professional nurses in executing these functions have undergone a rapid and continuous process of evolution among those who are professionally responsible for the care of the sick and injured.

Courts have held that professional nurses have a legal duty to interpret evidence presented by the patient possibly indicating the need for medical attention, and to proceed in the light of that interpretation to do what is required for the patient, as for example the need to call a physician [1]; to discontinue a treatment where there is evidence of its harmful effect, e. g., on an unconscious patient [2]; or to determine the patient's need for special medication, e. g., sedatives.[3] There can be little doubt that by custom and usage the relationship between doctor, patient, and nurse is one in which the parties recognize that the nurse as well as the physician has the function and responsibility to observe and interpret the patient's reactions.

The observation of symptoms and the making of a diagnosis imply the need for professional learning and mental acuteness. These functions are characteristic of the professional nature of nursing as well as medicine. The industrial nurse who observes the extent of illness or injury to an injured workman and determines whether she should render emergency treatment or wait until the physician arrives has made a vital diagnosis comparable in importance to many of those which physicians are called on to make. However, except for first-aid treatment and the employment of such measures as will prevent aggravation of the patient's

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injury or illness, the determination of therapy is within the exclusive domain of medical practice and beyond the limits of nursing practice.

Nurse's Malpractice

In *Cooper v. National Motor Bearing Co.*[4] the defendant appealed from a judgment in favor of the plaintiff in a malpractice action brought against a registered nurse and her employer.

In May, 1951, the plaintiff received a puncture wound on his forehead when another employee let a piece of metal slip from his hand. He went directly to the first-aid room and received treatment from the defendant nurse. She swabbed the wound with an antiseptic and put a bandage on it. According to the plaintiff's testimony she did not examine or probe the wound. He was told to return the next day which he did. The nurse again applied antiseptic but did not probe the wound. On the next day he also went to the dispensary, but on that occasion the nurse just looked at the wound.

On visits to the dispensary over a period of several months the plaintiff would point out to the nurse that the wound did not seem to be healing properly and she would say that if it did not she would have to do something. In March, 1952, the plaintiff visited the dispensary for a check of a chest injury and asked the nurse if she would send him to a doctor to examine his forehead. She referred him to a physician who excised a piece of tissue for laboratory examination. A pathologist examined the specimen and reported that it contained a basal cell carcinoma. On March 23, 1952, the plaintiff was operated on and a larger area was excised. Skin was removed from his right forearm and grafted to the forehead.

The plaintiff's case was tried on the theory that a metal splinter was left in the wound by the negligence of the nurse and that this foreign body, acting as an irritant, caused the cancer.

The nurse admitted that it was her duty to refer any condition or injury she was not familiar with, or sure about, to a doctor for diagnosis. The standard of good nursing care in the community required the nurse to examine the wound for foreign bodies. If splinters were too deeply embedded, the nurse was to send the workman to the doctor. The plaintiff's type of wound should normally have healed in about a week. If a wound persisted and did not heal, proper nursing care would require that the workman be sent to the doctor. The nurse admitted that she was familiar with the danger signals of cancer, one of which is "any sore that does not heal." Nevertheless she continued to treat the wound for 10 months before sending the plaintiff to the doctor.

In affirming the judgment of the trial court, the California District Court of Appeal said:

> a nurse's diagnosis of a condition must meet the standard of learning, skill and care, to which nurses practicing that profession in the community are held. A nurse in order to administer first aid properly and effectively must make a sufficient diagnosis to enable her to apply the appropriate remedy. Usually she receives some history of the accident or illness from the patient, inspects a wound, and bases her choice of treatment on the deductions thus made. She has been trained, but to a lesser degree than a physician, in the recognition of the symptoms of diseases and injuries. She should be able to diagnose, according to appellant nurse's own testimony herein, sufficiently to know whether it is a condition within her authority to treat as a first aid case or whether it bears danger signs that should warn her to send the patient to a physician . . .
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> Appellant nurse testified that it was the practice of a nurse in this type of industry to probe wounds for foreign bodies, that if there is a foreign body in a wound there is a feeling of sharpness on pressure, that according to the standard of care and her experience as a nurse, she should be aware of the possibility of foreign objects in such a wound.

If the plaintiff's cancer was the result of the nurse's failure to refer him to a physician for examination and treatment during the 10-month period during which she treated him, then it must be acknowledged that a judgment based on malpractice was proper. Employees as well as their employers are responsible for damages due to acts of negligence.

In other than emergency cases where a physician is not present, diagnosis is not a function of professional nursing and treatment by nurses is generally restricted to the execution of orders given by and under the direction or supervision of a physician. Furthermore, the nurse should only execute legally valid medical orders which she is qualified by training and experience to perform.

Nursing Functions

It is axiomatic that the practice of medicine may not be delegated to nonphysicians. Nevertheless there are numerous traditionally medical functions which are now also performed by nurses under the supervision or direction of a physician and recognized to be nursing functions. Accordingly, under the direction or supervision of a physician, a nurse may administer injections intravenously[5] or intramuscularly[6] or perform x-ray treatments.[7]

Basal metabolism tests, anticoagulant therapy, and the administration of blood transfusions and oxygen are now routinely performed by nurses. The great progress in the science of medicine has led to the delegation of numerous medical procedures to nurses. The first-aid equipment used by the industrial nurse today could have been used only by a physician not too many years ago.

On the other hand the order of a physician purporting to delegate to a nurse the authority to perform an abdominal operation, or an amputation, or to set a fracture or to perform any similar procedure would undoubtedly be considered invalid by the medical and nursing professions as well as the courts. In realistic terms, professional nursing practice includes not only emergency diagnosis and treatment but those medical acts and techniques which are commonly performed by qualified nurses under physicians' orders. Fundamentally, the scope of nursing practice is determined by medical custom. None of the statutes relating to nursing practice attempts to set forth the specific functions of nursing. This statutory flexibility has allowed for the rapid growth of nursing. Consequently the courts have been guided in identifying nursing functions by customs and practices of the medical profession, since physicians can best recognize the proficiency and attainments of nurses.

Emergency Treatment

A medical emergency may be defined as an unforeseen illness or injury which calls for immediate action for the safety of the patient.[8] Anyone, and not necessarily a professional nurse or a physician, may render first aid or perform medical acts to preserve life and limb in the case of an emergency. But one who renders aid in an emergency is under a legal duty to act as a reasonably prudent person. The qualified industrial nurse would generally be held to a greater degree of responsibility and skill than the layman, but to a lesser degree of responsibility than the physician.

Medical custom has permitted a broad definition of the term "emergency" to be applied. It ordinarily refers to situations requiring resuscitative or other first-aid measures. Guiding principles and procedures, approved by a responsible physician, are particularly useful to industrial nurses in such cases.

The case of *Burns v. Bakelite Corp.*[9] is a landmark court decision in the field of industrial nursing. It states the rule that an employer has a duty to provide emergency medical care and other assistance when an employee suffers a sudden illness while engaged in work. The court found that a registered nurse, acting on behalf of the employer, fulfilled this duty but many physicians and nurses may feel that the nursing profession is capable of maintaining a higher standard of performance than that demanded by this court. Because of its basic importance and interest, the holding and facts of the case are stated below in detail.

The plaintiff, who incidentally happened to be a trained nurse, alleged that the negligence of a registered nurse employed by the defendant was responsible for the death of her husband. The trial court judge before whom the case was tried took the case from the jury and rendered judgment himself for the defendant. In a jury case the trial judge is justified in doing this only "if fair-minded men could not differ" in their judgment.

The nurse, Mrs. B——, testified that on a certain morning the plaintiff, Burns, came to the dispensary, pale and perspiring, and she thought he looked ill. He complained of a severe chest pain and thought he had indigestion and he wanted peppermint for it. The nurse took his pulse and his temperature, and found both were normal. He had no difficulty in walking. The nurse suggested he see a doctor, but he refused to see the plant doctor whose office was only about two blocks away, and he asked for his own physician. The nurse tried unsuccessfully to reach the physician by telephone. Then the plaintiff asked her to send him home, and she summoned a car, a station wagon. Refusing assistance, he walked to the car and got in. By the removal of one of the station wagon seats, room could have been made for a stretcher, but the plaintiff was not put on a stretcher.

He was driven by the company's chauffeur to his home. The house was 50 ft. from the roadway, and to reach the front door it was necessary to mount seven steps. The chauffeur opened the door for the plaintiff and he got out and without aid walked to the house and climbed the stairs.

The nurse contacted the plaintiff's doctor soon after the plaintiff had left the plant but he was engaged in an operation and sent a colleague. The doctor gave a diagnosis of coronary occlusion. He was taken to a hospital where, six days later, he died. The opinion of the court states:

> Generally, no duty rests on an employer to provide medical service or care for an ill or injured employee. Yet when the employee, while engaged in the work of his master, suffers a sudden illness that renders him unable to provide for his own care, the employer must put in his reach such medical care and other assistance as the emergency thus created may in reason require. The duty arises out of necessity. . . .
>
> The symptoms that the nurse observed were typical of the onset of a heart attack, although they might indicate acute indigestion or some other condition. But a physician would probably have made a tentative diagnosis of a "coronary occlusion" because that is the most common cause of such symptoms. Based on that diagnosis, the standard emergency treatment would have been the administration of morphine to relieve the pain, not only for the patient's immediate ease but because the pain causes reactions in the heart that increase the damage to that vital organ. And the patient should not be permitted to walk or to make avoidable physical effort. But Mrs. B—— is not a physician; she did not realize that Burns was suffering from a coronary thrombosis; she only knew he was ill and he did not appear to her to be seriously ill. Even if the nurse had made a diagnosis of heart attack, she was not authorized to administer morphine, for such drugs are administered only after the direction of a licensed physician. . . .
>
> There is no negligence indicated by Mrs. B——'s failure to recognize the particular ailment from which Burns was suffering. But should the various symptoms that she observed and that we have recited have warned her it was dangerous to allow Burns to be taken home in the station wagon? If so, there was a failure to exercise due care. If fair-minded men, after carefully considering the facts, could differ in their answer, then the question should have been left to the jury. . . . Run over the facts again—face pale, perspiring, severe pain in chest, pulse and temperature normal, walked without difficulty; the man himself thought he had indigestion; the nurse thought he looked ill, but not very ill. In our opinion, there

> was nothing to suggest that he was a stretcher case, or that there was need for other means than those employed, or for more care than was exercised in sending decedent home. We find no error in the award of judgment to defendant.

The significance of the case is that it recognizes the duty of the industrial nurse to make a tentative diagnosis of the patient's condition. The nurse was not held to the standards of diagnosis required of a physician, although the court felt that the symptoms were such that a physician would probably have made a tentative diagnosis of a heart attack. Actually, many industrial nurses would probably have suspected the symptoms in the case as common symptoms of a heart attack.

Summary

The profession of nursing is a dynamic discipline which embraces an ever-increasing number of functions. Nurses, particularly those employed in industry, should be careful to limit their diagnostic and therapeutic activities to emergencies and to avoid continued treatment of a patient unless such treatment involves the carrying out of the specific orders of a physician who is in charge of the case.

Under the direction or supervision of physicians, nurses are performing as nursing practice numerous procedures which were formerly performed exclusively by physicians. The limitations on the procedures which a nurse may properly perform are governed by (*a*) the nature of the relationship between the medical and nursing professions in the community, (*b*) the scope of training offered in recognized nurses' training schools, and (*c*) the training, experience, and proficiency of the individual nurse.

In emergency cases, industrial nurses have a duty to determine the need for prompt medical attention, to make a tentative diagnosis of the patient's condition, and to employ necessary resuscitative and first-aid measures.

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A PRUDENT WAY OF LIFE.—Perhaps Sir Thomas Lewis' description of a prudent way of life would not appeal to some of us, but its practice would no doubt be a forward step in the control of our nation's number one public health problem. "Very prudent people," said Lewis, "live quietly and moderately; they have their simple daily routine of work and pastime, enlivened by occasional excursions and entertainments, social gatherings and visits to and from their friends. They are temperate in their eating, taking no more than will maintain them in robust health, arranging their diet to consist chiefly of plain good food, relieved occasionally of its monotony by a more elaborate, but not heavy meal. They are regular in their habits of work and exercise, and in their mealtimes. They are strictly temperate in their drinking. They control their emotions and their passions. They avoid all forms of excess. They use tobacco little if at all. They welcome the freshness of abundant air and open spaces, delighting in the feelings of invigoration that accompany active exercise; they love the warmth of sunlight playing on their skins and the sleepiness of healthy fatigue. These are habits that few people in industrial countries now adopt, that fewer still maintain. The cares and distractions of an increasingly complex life, indoor or sedentary occupations, advancing years and the decreasing energy interfere less or more, and the prudent rules are neglected; neglect is the easier because the penalties, owing to the body's great power of resistance to disease, are uncertain in their incidence and often long deferred." Healthy habits would become more prevalent if the consequences of their neglect were more immediate and variable. Indeed, healthy habits, an optimistic philosophy, and the sound use of the abundant leisure which has made us the envy of the world, might well neutralize or retard the atherogenic mechanisms which are both initiated and accelerated by the "stress and strain" of our daily struggle for existence.—H. I. Russek, M.D., Emotional Stress and the Etiology of Coronary Artery Disease, editorial, *The American Journal of Cardiology*, August, 1958.

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AMMONIA TOXICITY AND HEPATIC COMA

HEPATIC COMA, characterized by a flapping tremor, disturbed consciousness, and electroencephalographic changes, may occur in patients with cirrhosis of the liver or with portacaval shunts.[1] It is generally believed that under such circumstances toxic substances absorbed from the intestine may escape the normal detoxification processes in the liver and hence enter the systemic circulation and reach the brain. The identity of the toxic agent (or agents) in hepatic coma has not been fully established, but considerable evidence has accrued to implicate ammonia in this respect. Ammonia is normally present in appreciable amounts in the portal vein, due to intestinal absorption of ammonia derived from the bacterial breakdown of nitrogenous foodstuffs. Ordinarily this ammonia, together with the endogenous ammonia arising from the deamination of amino acids, is converted to urea by the liver, but in the presence of liver disease, or if the liver is bypassed, appreciable amounts may enter the systemic circulation. Blood ammonia levels are usually elevated in hepatic coma and coma may be precipitated in susceptible persons by the administration of ammonium salts or urea or by other factors capable of elevating the blood ammonia level such as a high-protein diet or gastrointestinal hemorrhage.[2] Additionally, avoidance of nitrogenous foodstuffs,[3] alterations in intestinal flora by chemotherapeutic agents,[4] or the removal of blood ammonia by dialysis [5] may result in clinical improvement.

Despite the apparent association between ammonia toxicity and hepatic coma, it has repeatedly been observed that blood levels of ammonia do not always reflect the severity of the symptoms of hepatic coma or the development of electroencephalographic changes.[6] A possible explanation of such discrepancies has recently been advanced by Warren and his associates.[7] These investigators postulated that, since ammonia is a weak base and since weak acids and bases are known to penetrate the blood-brain barrier largely in un-ionized form, the cerebral toxicity of ammonia should be influenced by the pH of the blood. In substantiation of this, they injected a number of ammonium salts (chloride, acetate, bicarbonate, and carbonate) into mice and found that the toxicity of the salts increased in direct relation to their ability to increase the blood pH. Further, when the LD_{50} of the various ammonium salts was injected into the animals, the brain ammonia concentrations proved to be essentially the same for each salt although the blood concentration of ammonia varied directly with the dosage, thus indicating that the lethal effect of ammonia is cerebral in origin. It was concluded that as the blood pH was increased by the injected salt the amount of un-ionized ammonia (NH_3) was increased relative to that of the ionized (NH_4^+) form. Since the normal blood pH is quite close to the pK of ammonia, small shifts in blood pH could be expected to significantly affect this ratio of un-ionized to ionized ammonia and hence profoundly influence the degree of penetration of the blood-brain barrier by the ammonia. Indeed the data reported indicate that changes of pH in the order of 0.1 unit result in a 50% rise in the concentration of ammonia in the brain. Such a phenomenon would explain the recently reported association of coma and alkalosis in patients with elevated blood ammonia levels [8] and the increased tolerance to infused ammonium observed in dogs receiving 10% carbon dioxide.[9] It also suggests that acidifying agents may be valuable adjuncts in the treatment of hepatic coma and indicates the futility of attempting to correlate the degree of cerebral intoxication by ammonia by determination of blood ammonia levels without taking into account the blood pH.

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ORGANIZATION SECTION

REPORT OF THE COMMITTEE TO STUDY A. M. A. OBJECTIVES AND BASIC PROGRAMS

TO THE HOUSE OF DELEGATES AT THE CLINICAL SESSION, DEC. 2-5, 1958, MINNEAPOLIS

In our progress report to the House last June in San Francisco, we stated that our Committee was appointed by the Speaker pursuant to an action of the House in Philadelphia (December, 1957) modifying the recommendations of the Hyland Committee which earlier had been assigned the task of analyzing the report of the management consulting firm, Heller and Associates. Members of the House will recall that our Committee was requested to study four subjects: (*a*) redefinition of the central concept of A. M. A. objectives and basic programs; (*b*) placing more emphasis on scientific activities; (*c*) taking the lead in creating more cohesion among national medical societies; and (*d*) studying socioeconomic problems. This report sets forth our Committee's recommendations on these four topics.

At the conclusion of our report you will find the questionnaire and the two-page statement, "Genesis of the Committee," attached for your information. Inasmuch as all members of the House received the questionnaire, its inclusion here is merely for reference. Following the questionnaire itself are two long appendixes prepared for us by the Bureau of Medical Economic Research. Appendix A sets forth more than 1,600 quotations selected from the returned questionnaires. These actual words may mean as much to some members of the House as the statistical analysis of the returned questionnaires, which is the subject of Appendix B. In the latter, we would especially call your attention to the tests of the representativeness of the respondents to the questionnaire sent to a probability sample of physicians, members and nonmembers. These tests indicate that the respondents were so representative that replies from one or two thousand more respondents would probably have given the Committee very little additional information.

During our second meeting in San Francisco last June, the Committee reviewed progress on the survey, decided not to undertake a series of depth interviews, and made plans to terminate its investigation in order that the final report could be presented at the Minneapolis meeting. Our first meeting was held on March 15 of this year. The third meeting of the Committee was held in Chicago on Sept. 5 and 6 at which time this report was completed.

Your Committee's report is based on many informal conversations by members of the Committee, personal correspondence, the 1,600 selected quotations (Appendix A), the statistical analysis (Appendix B), and some 90 letters attached to the returned questionnaires. We are not reporting the results of a scientific opinion poll. The Committee wishes to make it clear that this report represents the views of the six members of the Committee aided by the materials furnished to it. At this time, we wish to thank the many members of the Association and a considerable number of nonmembers for their assistance.

The Setting

The Committee wishes to point out that any consideration of the four matters referred to it is circumscribed by the times in which we live. Medicine itself is changing rapidly; so rapidly that it seems to be exploding in many directions. The pace of advance in the science and art of medicine constantly amazes all of us. A year seldom passes without a new medical organization or health agency being born. Performance over a period of years may be necessary to determine whether these new organizations or agencies are genuinely medical or largely devoted to fund raising. This rapid pace of change has many other manifestations in our field of endeavor. Indeed, historians may record that the greatest accomplishment of the 20th century was that men learned how to die old instead of young. Apparently this greatest period of rapid mortality decline has run its course as the expectation of life at birth is now creeping upward very slowly from 69 years to 70 years. A continuation of the earlier rapid rise in this important statistical measure of life awaits further important developments in the medical management of the diseases of older life.

You have directed us to reexamine four important aspects of our Association. Every professional organization needs an occasional reevaluation. Your request comes at a time when the success of medicine in terms of length of life has reached a high and, at present, a rather stable level. For these great gains in the length of life the American people are grateful to us and to our fellow scientists. In our analysis of our Association, we have steadfastly kept in mind that the unique function of our profession which has distinguished it from other professions is that we have life on our hands. We are also mindful that in recent years medicine may

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The historical background and appendixes to the report are available for study on a loan basis and may be secured by writing to the American Medical Association, Economic Research Department, 535 N. Dearborn St., Chicago 10.

have suffered more from its successes than from its failures. Progress in postponing death has come so rapidly in the past several decades that we must now recognize that the rate of progress can scarcely be continued at its frenzied pace. We make these brief observations in this preamble because these and other great factors are a part of the pattern provided us by our times; the problems of the American Medical Association are very much a part of the entire American scene. There are, of course, many socioeconomic factors involved even as there are in other fields about us. Among these are technology, industrialization, urbanization, unionization, inflation, and the rising percentage of older voters.

Asking for Criticism

When any long-established organization attempts rigorous self-criticism, some of its members and many outsiders may lift their eyebrows and question that it can be done. However, we submit that our attempts to obtain criticism have been highly successful. We have read and heard both favorable and unfavorable criticisms of every major activity of the Association and of every Headquarters' department; some were stated in rather vigorous language. The Committee is not confronted with an undersupply of criticisms. Moreover, the Committee is now convinced that a survey of the type such as we have conducted should be repeated every three or five years. In general, we would like to reassure the House that the volume of information we have received is quite sufficient for our purposes. Our problem is to utilize this wealth of material most effectively.

A few general comments on these preliminary observations seem warranted. Your Committee has been impressed with the great variety of ideas expressed. Interesting side lights have also been noted. For example, some of the extreme criticisms we received remind us of the young socialist who liked to banter his opposition with "I have a plan for increasing government control in the field of medicine. You don't have a plan for more government control. Therefore, I am doing positive thinking and your approach is negative and reactionary." Another side light was the unusual suggestion of a few respondents that the A. M. A. should immediately develop and insist on a minimum wage for interns and for residents. It will repay one to read all the 1,600 selected quotations in Appendix A. You will note many other side lights.

If it can be said that these many and varied criticisms point in any central direction, it would be that the central problem of our Association in the year 1958 is "splintering"—the dynamics of medicine are driving us in so many directions simultaneously. The result is more and ever more divisions and subdivisions in the practice of medicine. One may justly ask, is medicine organized or disorganized? The central imperative for our Association is to re-establish its leadership, and unify the fragments into a cohesive entity under one umbrella.

The Questionnaire Survey

Copies of this report, together with the appendixes, were mailed to the members of the House several weeks in advance of this meeting. We may now turn to a review of the questionnaire survey on each of the four topics assigned to us by the House. These topics were captioned A, B, C, and D in the questionnaire. Additionally, we include our findings and recommendations. At this point in our report we shall consider only the highlights of the statistical analysis of Appendix B.

During May our questionnaire was mailed to all members of the House and alternate delegates. It was also sent to the officers and trustees, 13 past-presidents, the editors of state and county society journals, the secretaries or executive secretaries of state and county medical societies, the secretaries of the American Boards, the national organizations of medical interest (listed periodically in THE JOURNAL), the deans of medical schools, and members of A. M. A. councils and committees. We shall refer to these as the black questionnaires because they were printed in black ink. Of this total of 2,938 mailed, 521, or 18%, were returned by the cutoff date for key punching and tabulation, July 11. (Actually 522, not 521, black questionnaires were used in the statistical analysis; see the first table in Appendix B for the number of usable returns and requested questionnaires.) The county medical societies accounted for 1,904 of the 2,938 black questionnaires mailed; 245 replies or 13% were returned; excluding the questionnaires sent to the county societies, the return was 27%. The members of the Committee were puzzled by the 34% return from the members of the House. However, we do recognize the pressures of time and circumstance, and are confident that the response obtained reflects a dependable consensus of that body.

The same questionnaire was printed in blue ink and mailed to 3,924 members and nonmembers, a probability sample, consisting of every 60th name in the punch card file. Only 497, or 13%, were returned; and 32 were unusable. Frankly, the Committee had expected a higher percentage of returns, considering the amount of publicity given to the project. The two most important explanations are that this type of request for criticism of the Association is new and the four topics assigned to the Committee and incorporated in the questionnaire are inherently difficult. The Committee was greatly pleased, however, by the wide scope of the replies as indicated by the selected quotations of Appendix A. Moreover, as set forth in detail in Appendix B, the 465 respondents to the blue questionnaire were a good cross section of the entire probability sample of 3,924 members and nonmembers as to age and state of residence. (The black questionnaires were sent to a stratified sample of persons holding certain positions.) Although the Committee was not trying to take a poll, the representativeness of the relatively small number of respondents to the blue questionnaire strongly suggests that a larger response would have added little to the Committee's knowledge. Over and above these technical considerations, your Committee recognizes that its task was to weigh and interpret the specific criticisms received and present to this House a series of observations and recommendations on each of the four topics assigned to it. Although our report will review the results as if there were four separate compartments corresponding to the four separate assignments given the Committee by the House, certain types of comments appear and reappear among the responses to all questions; for example, comments of a socioeconomic nature appear in the responses to every question although the Committee designed Part D for that purpose.

Part A

(Redefinition of the central concept of A. M. A. objectives and basic programs.)

The Committee instructed the staff of the Bureau of Medical Economic Research to break up each question, particularly those requesting comments, into a series of subquestions or categories to be phrased by the Bureau staff after an examination of several hundred replies. In editing the replies to Part A, it was found that 13 subquestions or categories could be used in coding and editing the replies to all three questions (see list of subquestions in Appendix A):

1. What is your idea of what the A. M. A. does for you? For the American public?
2. What do you think the objectives, aims, and goals of the A. M. A. should be?
3. Do you have suggestions for improving the service and effectiveness of the A. M. A.? Yes ☐ No ☐ If yes, please give them.

For example, many of the suggestions for improving the service and the effectiveness of the Association under question 3 were very similar to what other respondents suggested as the objectives, aims, and goals in question 2. Likewise, some of the respondents gave objectives, aims, and goals requested under question 2 in their replies to question 1 about what the A. M. A. does for you and for the American public. This same intermingling of questions 1, 2, and 3 was also noted in the 90 letters attached to the returned questionnaires. Thus, the responses to the three questions of Part A were considered under 13 subquestions or categories thereby displacing the original three questions. The essential unity of Part A has been preserved, but the separate quality of the three questions thereunder is somewhat blurred by this procedure. The five categories or subquestions mentioned most frequently by the respondents were numbered 2, 4, 5, 6, and 9.

2. *Scientific Information:* Improving, advancing. Dissemination to physician. Physician's informal post-grad. Publications, J. A. M. A., advertising. Scientific assemblies, exhibits. Research.

4. *Practice of Medicine:* Standards; maintaining or improving. Protection of M.D. Prestige. Osteopaths, relations with.

5. *Organization of Profession:* Leadership, official representation, coordination. Spokesman for profession, spokesman for physicians. Parent organization. Integration of groups within A. M. A. (e. g. Specialty and G. P.). Inter-group relationships within profession. Medical policies; positive vs. negative stand. Communication, county and state societies, and national level.

6. *Socioeconomic and Political Areas:* Study and dissemination of information. Representative spokesman for profession. Lobby. Physician's union. Socioeconomic and political policy. Cooperation with other professions and self-employed groups. Free choice of physician. Socioeconomic problems. Distribution of physicians. Cost of medical care. Insurance.

9. *Medical Care for Public:* Advancing, improving, individual and public health. Protection against quacks, improper drugs. Investigations.

The typical respondent to each of these questions mentioned two of these 13 categories or subquestions. In giving the replies to the three questions, 987 respondents "checked" a total of 5,726 of these 13 categories or subquestions. A total of 1,113 mentioned some objective or activity of a socioeconomic nature (number 6); 851 mentioned some phase of the organization of the profession (number 5). The differences in the rank order of the tabulations for the black and the blue questionnaires were not very marked. Among the black questionnaires the third most frequent response dealt with medical care for public (number 9), but practice of medicine (number 4) ranked third among the blue questionnaires. The subquestion or category ranked fourth among the black questionnaires was scientific information (number 2); among the blue questionnaires, medical care for public (number 9). Although the tabulations of these three questions set forth in Appendix B are worth study for the details provided, we conclude at this point that insofar as the responses received in our questionnaire survey are concerned, the socioeconomic function of our Association looms largest in the minds of our members. The 90 thoughtful letters and the reflections of the Committee further substantiate this conclusion.

As a result of these observations, your Committee concludes that the membership of the A. M. A. is convinced that the sociological and economic trends and conditions of today constitute an important aspect in the medical care of the patient and of the practice of medicine. Along with medical education, diagnostic medicine, therapeutic medicine, preventive medicine, Public Health medicine, and medical research—the art and science of medicine—sociological and economic aspects are integral parts of the unlimited health care of the people.

We, therefore, recommend that this House of Delegates consider the advisability of amending Article II of the Constitution by this substitution:

"The objectives of the Association are to promote the science and art of medicine and the betterment of public health, and an understanding of the socioeconomic conditions which will facilitate the attainment of these objectives."

Additional suggestions in the socioeconomic area are presented later in this report.

Part B

(Placing more emphasis on scientific activities.)

The second area, Part B, which the Committee was asked to investigate was scientific activities. Our broad interpretation of this was that we were to advise the House as to whether the scientific activities of the Association were generally adequate, generally inadequate, or about right. This was a large order for the questionnaire which we wanted to limit to 10 questions. (As has been pointed out already, some of our best information on one of the four parts of the questionnaire was actually included in the reply to another part.) The three questions follow:

4. Does the present degree of emphasis placed upon scientific activities by the American Medical Association meet with your approval? Yes ☐ No ☐ (Comments regarding specific activities will be appreciated by the Committee.)

5. Have you attended a midwinter Clinical Session? Yes ☐ No ☐ Do you consider these sessions valuable?

6. The Committee solicits your comments, if you have any, on the work of the A. M. A. bureaus, committees, councils, departments, divisions, and other agencies listed below. Please attach a reply if the lines provided below are not sufficient.

1. Bureau of Health Education
2. Bureau of Medical Economic Research
3. Committee on Legislation
4. Council on Constitution and Bylaws
5. Council on Industrial Health
6. Council on Medical Education and Hospitals
7. Council on Medical Service
8. Council on Mental Health
9. Council on National Defense
10. Council on Rural Health
11. Council on Scientific Assembly
12. Department of Public Relations
13. Division of Councils of Therapy and Research
    14. Council on Drugs
    15. Council on Foods and Nutrition
    16. Council on Medical Physics
    17. Bureau of Investigation
    18. Chemical Laboratory
19. General Manager's Office
20. Law Department
21. Judicial Council
22. Records and Circulation Department
23. Scientific Publications & Library
24. Today's Health
25. Washington Office

Of the returned black questionnaires, 86% indicated that the present degree of emphasis on scientific activities met with the approval of the respondents; the percentage on the blue questionnaires was 76. This overwhelmingly affirmative reply from those who chose to respond does conceal some of the important observations which the members of the Committee have read in the selected quotations in Appendix A. A few respondents claimed that many papers in The Journal were apparently chosen on the basis of when and where delivered rather than content and that the journals and the meetings of the specialty organizations were more valuable from the scientific standpoint.

In the matter of the Clinical Session, the number responding to the black questionnaire who had attended and who had not attended a clinical session was about equal, whereas the respondents to the blue who had not attended were about two and one-half times as numerous as those who reported they had attended. On the question of whether the midwinter Clinical Session is valuable, the ratio of "yes" to "no" on the black questionnaire was 5 to 1; and 4 to 1 on the blue questionnaire. In both groups, however, one-third to one-half did not reply.

The major purpose of question 6 was to set forth the 25 bureaus, committees, councils, divisions, and departments. Unfortunately, this question was left blank on more than half of the black and the blue questionnaires; fewer than one-third made specific comments on one or more of the 25 listed agencies of the Association. (See selected quotations in Appendix A.) A number of respondents wrote that this list of 25 agencies was an education to them; indeed, this was the primary purpose of the Committee in listing them. It was also felt that this list of 25 agencies might help respondents in answering other questions. Typically, respondents on the black questionnaire who gave a specific reply referred to three of these agencies and those on the blue questionnaire to two. It was very difficult to edit and code the responses to this question which might be said to have 25 parts. The first attempt was to classify the responses as favorable or unfavorable for the agency concerned. For example, consider a respondent who after indicating disagreement with a specific A. M. A. policy severely criticized the agency which published items in support of that policy. Should this reply be considered favorable or unfavorable criticism of the specified agency? Since no agreement could be reached on a consistent pattern of interpretation of comments as being favorable or unfavorable and the replies were so few, the Bureau of Medical Economic Research was asked merely to tabulate the number of mentions of each of the 25 agencies. Despite the small number of replies, it may be helpful to note that the Council on Medical Education and Hospitals, the Department of Public Relations, the Washington Office, and the Council on Drugs were mentioned (favorably or unfavorably) most frequently.

The conclusion of Part B on the subject of whether our Association should or should not place more emphasis on scientific activities is that there are no widespread dissatisfactions with the Association's present emphasis on scientific activities as a whole, so far as is revealed by a mere count of the replies of the respondents. But the selected quotations (see Appendix A) and our own observations indicate some measure of dissatisfaction. Scientific progress is never-ending. Your Committee strongly advises the Board of Trustees to give serious consideration to the establishment of some more effective mechanism to insure continued study of the scientific activities of the Association with the ultimate intent and purpose of revamping and otherwise changing them as deemed necessary. Your Committee understands that there is already a "special committee to study scientific activities," but it is believed that the scope of the "special committee" is too limited. This thought about the scope of a study of scientific activities of the Association will be more fully developed in a section of this report to follow.

Part C

(Taking the lead in creating more cohesion among national medical societies.)

The third part of the Committee's assignment was to examine the need for creating more cohesion among national medical societies. Questions 7 and 8 of Part C were designed to provide the Committee with specific advice on this problem of the relationship of our Association to other national medical organizations with an invitation for comments on question 7, but not on question 8.

7. Do you approve of the present relationship between the American Medical Association and other national medical organizations? Yes ☐ No ☐ (The Committee would welcome your suggestions for changes in the relationship of the A. M. A. to a named national medical organization[s].)
8. Do you believe that independent action among national medical societies promotes or impedes progress toward the goals of the medical profession? Promotes ☐ Impedes ☐
If you believe that more cohesion among national medical societies is desirable, please indicate in which of the three areas: Scientific ☐ Socioeconomic ☐ Both ☐

Among the respondents to the black questionnaire a ratio of better than 3 to 1 approved the present relationships; check marks on the blue questionnaire agreed with the ratio of more than 3 to 1. This was a very general appraisal of our relationships with the other national organizations. Although the comments offered in addition to the check marks were fewer than we had hoped, it is apparent that some respondents doubt that the A. M. A. is still the recognized leader of the profession. This type of comment was also given in Parts A and B. Others believe that more coordination is desirable particularly in regard to the meetings of the other national organizations—a comment which might have been given to question 8 if the Committee had provided lines for comments. There was a wide scatter of other comments, but the relationships with the American College of Surgeons and the American Academy of General Practice were featured. The phrases excerpted from the comments on question 7 provided the Committee with some illuminating details.

The Committee sought to obtain additional light on this problem of relationships by asking only for check marks in question 8. The replies on the black questionnaire produced a tie on the question of whether independent action among national medical societies promotes or impedes progress toward the goals of the medical profession. Recognizing that we are reporting to you information derived from a small sample, we believe that this even division between the pros and cons is worth noting. Among the respondents to the blue questionnaire, the ratio was about 3 to 2, three "promotes" and two "impedes." In our desire to offer you a few objective questions requiring only check marks for your answers we did not invite comments regarding what "promotes" and what "impedes" progress toward our goals in the first part of question 8. The Committee was aided, however, by comments on the question of relationships with other national medical societies which were recorded among the responses to other questions.

From the replies to this second part of question 8 it is clear that the respondents believe that more cohesion is needed in both scientific and socioeconomic areas, with somewhat more stress on the latter. Moreover, the respondents to the black and the blue questionnaires were generally in agreement, although the latter placed slightly more stress on the scientific areas than did the former. In other words, the respondents, whether they thought independent action promotes or impedes progress toward the goals of the medical profession, told us that more cohesion among national medical societies is desirable. In the light of what the Committee learned from the responses to Part C, from the phrases excerpted from the replies to the other parts of the questionnaire, and on the basis of our own observations and discussions with a wide variety of physicians, we recommend that a more thorough study should be made of our relationships with other national medical organizations with a view to improving them and to reasserting A. M. A. leadership in socioeconomic areas particularly and to the maximum extent in scientific areas.

In order to accomplish these objectives, we recommend that the Board of Trustees in establishing a mechanism for the continued study of the scientific activities of the A. M. A. insure that that mechanism will assume the responsibility for establishing active liaison with each national medical society. The intent of this liaison should be to explore all fields of interrelationship between the A. M. A. and the national medical societies. There should be an attempt to define the area of activity of each organization. In the scientific fields the role of the A. M. A. might be primarily that of coordination between the special fields of scientific interest of the other national medical organizations. Improved cohesion between these organizations and the A. M. A. could result if the A. M. A. were to abolish its scientific sections and invite these national organizations to furnish the specialty and General Practice programs at each annual session. This possibility at least deserves study, and if it were to prove practicable, the participating other national medical organizations might be given the representation in the House of Delegates vacated by the scientific sections as they are abolished.

In view of the many comments in Appendix A concerning the voluntary health agencies, it is equally important to insure that the mechanism for continued study of scientific activities of the Association include provision for the establishment of close liaison with those health agencies for the mutual benefit of the agency, the profession, and the public.

Part D

(Studying socioeconomic problems.)

The fourth part of our assignment was to study socioeconomic problems. As already noted, comments of a socioeconomic nature were prominent in the responses to Parts A, B, and C of the questionnaire. So great was the ground swell of comments of this character that we could not compartmentalize them in Part D. Question 9 was our second objective type question requiring a Yes or No answer, on a choice of three socioeconomic policies.

9. How far should the A. M. A. go in the socioeconomic field? Please check one of the following three: a. Should the A. M. A. limit itself to matters of prime concern to the health of the people of the nation? Yes ☐ No ☐. b. Or should the A. M. A. interest itself in socioeconomic factors of America which affect the health of the people of our nation and the practice of medicine? Yes ☐ No ☐. c. Or should the A. M. A. also interest itself in socioeconomic issues whether or not they directly affect the health of the people of our nation or the practice of medicine? Yes ☐ No ☐

10. What socioeconomic policies of the A. M. A. do you approve or disapprove?..

A number of respondents answered more than one of the three, but the overwhelming proportion of check marks on policy "b" provided us with a definitive answer.

Socioeconomic policy "a" was not popular. In the black questionnaires the single responses were 35 to "a," 281 to "b," and 93 to "c"; considering respondents who checked more than one answer, those stressing policy "a" numbered 57, "b" numbered 364, and "c" numbered 154. The responses on the blue questionnaires present substantially the same result with great emphasis on policy "b."

Your Committee concludes, therefore, that the A. M. A. should not "limit itself to matters of prime concern to the health of the people of the nation." It should "interest itself in socioeconomic factors which affect the health of the people of our nation and the practice of medicine." Supported by the results of the returned questionnaires and other sources, we would conclude that the A. M. A. should not interest itself in "socioeconomic issues whether or not they directly affect the health of the people of our nation or the practice of medicine." We submit that a comprehensive history of the American Medical Association would indicate that policy "a" was favored in an earlier era. Indeed, we believe that policy "c," the almost unbounded scope of socioeconomic interest, may well be the policy toward which our Association is now moving. Obviously, a constantly increasing number of our members realize that good health is dependent not only upon good medical care but also upon good food, good clothing, good housing and good sanitation as well, and that their dual responsibility as physician and citizen makes imperative an active participation by their Association in any and all legitimate activities directed toward that goal. We commend these findings to this and future sessions of the House of Delegates without specific recommendations for changes in the Constitution or the establishment of a 10-point or 20-point socioeconomic program.

The tremendous emphasis in this questionnaire survey on socioeconomic policies was one of the surprises to our Committee. It seems that no matter which questions we asked about objectives and policies, and/or how we worded them, the socioeconomic aspects were somehow emphasized by respondents. (See Appendix B.) No longer can it be claimed that our Association is not interested and should not be interested in socioeconomic factors of American life.

In framing question 10 the Committee thought it wise not to specify socioeconomic policies by name. Responses indicating general approval, though few in number, greatly exceeded responses indicating general disapproval of Association policies. Almost half of the respondents commented on one or more specific policies. In coding and editing the responses, 19 policies were mentioned often enough to warrant tabulation. As stated in the preamble, we consider it of critical importance that the House positively know this to be a committee's report and not a statistical report of the results of a scientific poll of opinion. Hence, it would serve no purpose to report on the tabulations separately for and against a specific policy. Approval or disapproval of the Association's stand on socialized medicine was mentioned most frequently, with approval or disapproval of the Association's position on social security coverage for self-employed physicians ranking second, followed by approval or disapproval of Association policy on the extension of voluntary health insurance. The fourth most popular item was approval or disapproval of what we were forced to call "publicizing policies." As noted, many of the responses to other questions have provided useful information to the Committee on socioeconomic policies. Curiously, the Forand bill and the third party problem ranked below all four of these policies.

Part E

(Classification of Respondent.)

The last section of this questionnaire survey, Part E, provided for the classification of the respondent. As shown in Appendix B, the distributions by age and by state of those who responded to the blue questionnaire and those who did not respond were quite similar. Although the IBM punch card file could not be used for testing the representativeness of the respondents as to type of practice, form of active private practice, and size of city, the fact that the distributions by age and by state were reasonably similar suggests that the respondents were representative of the entire group of 3,924 in the probability sample to whom blue questionnaires were mailed. This fact fortifies the Committee's confidence in the questionnaire survey results. Since the black questionnaires were sent to a stratified sample in which the number of county medical society secretaries loomed so large, a similar test of the representativeness of the respondents to the black questionnaires was not even attempted.

Most of the respondents on the black questionnaire reported that they are A. M. A. members, as did more than four-fifths of those who responded to the blue questionnaire in the probability sample. We are pleased to report that 9 out of 10 respondents to the black questionnaire signed it; and 8 out of 10 who responded to the blue questionnaire did likewise.

General Conclusions

In the foregoing we have set forth our findings, suggestions, and some recommendations on each of the first three topics which you assigned to our Committee. We turn now to more general conclusions including our recommendations on the fourth topic.

First, the members of the Committee were in unanimous agreement that it should be discharged although the task is not finished. Indeed, our studies definitely indicate this to be a continuous task. A reasonably complete set of recommendations would require more study and consideration of the setting provided by the rapidly changing medical, economic, social, and political events of our times, such as a continuous study would eventually reveal. Periodic self-examination is highly desirable, especially at this juncture in the development of our Association, the practice of medicine, and the rapidly changing social scene in the United States.

Second, we recommend the establishment for a period of three years of a Council or Committee on Socioeconomics to investigate socioeconomic and related problems with which the Association is likely to be confronted in future years. This council or committee could be of five members who should be appointed by our President, the Speaker of our House, and the Chairman of our Board of Trustees. This council or committee should have power to hold conferences with any and all individuals or groups who might develop ideas of aid to our Association and its purposes. This council or committee should report to the Board of Trustees and to the House of Delegates. During its three-year tenure, this committee or council should find its place in our Association activities and the House and Board of Trustees should review its work thoroughly before its activities are continued beyond the three-year period. Your Committee hopes that the materials we have provided will chart a course for this new council or committee.

Third, your Committee recommends that the Board of Trustees give serious consideration to opening the publications of the Association to a free and open discussion of socioeconomic problems *applicable to medicine. Members and officers* of the Association should be encouraged to contribute items to this section of the publication, or publications; and a special invitation should be extended to the many able persons on our Headquarters' staff. In the words of a member of our Committee, "We must restore to our members the feeling of belonging." We must not stifle constructive criticism; forward-looking discussions of any and all future problems should be made available to our members.

The Committee is thoroughly convinced that the A. M. A. must vigorously reassert its leadership in American medicine. We must cease the splintering tactics so disastrous to French politics. We must not become a disorganized profession. A more vigorous and more deliberately developed socioeconomic program toward this end is imperative.

At this point, your Committee wishes to direct special attention to the time-consuming, painstaking, thoroughgoing, and most effective work performed by Dr. Frank G. Dickinson and his staff, Dr. Leonard W. Martin, research associate, Olga Stetsuk and Cynthia Harkness, research assistants, of the Bureau of Medical Economic Research.

From the outset of our activities, Dr. Dickinson gave us expert counsel and guidance in the preparation of the questionnaire and in the method of its distribution among our members and nonmembers. In innumerable other ways he brought to our activities the experience and perspective of the expert statistician which are invaluable to any survey; but particularly so in the sensitive area of socioeconomic policies applicable to the American Medical Association.

We would especially emphasize the manner in which Dr. Dickinson and his staff have analyzed the responses to the questionnaire, have broken them down into subquestions, and have catalogued these responses in a manner designed to make our task much easier and our report more meaningful. The selection of some 1,600 quotations from the returned questionnaires—an ingenious procedure—presented in Appendix A has made us feel that the respondents were invisible members of our Committee. The statistical analysis of the returned questionnaires (Appendix B) reflects the consensus of an important cross section of informed and interested physicians throughout the country.

Finally, we wish to thank again all members and nonmembers who have counseled with us, those who returned their questionnaires, and particularly those who wrote us the 90 letters of more than 180 pages.

JAMES Z. APPEL
THURMAN B. GIVAN
HUGH H. HUSSEY JR.
RAYMOND M. MCKEOWN
MILFORD O. ROUSE
LEWIS A. ALESEN, *Chairman*

REPORT OF REFERENCE COMMITTEE

Report of Committee to Study A. M. A. Objectives and Basic Programs.—Your reference committee has spent an unusual amount of time in studying the report of the Committee to Study A. M. A. Objectives and Basic Programs and in listening to the free discussion in the open session. Truly heartening is the tremendous interest manifested by the respondents to the questionnaires, by oral discussions in small groups, and by the spirited review before the reference committee. It may be that this report will be a most significant milepost in the history of the American Medical Association.

With the far-reaching changes that have evolved in the socioeconomic and political areas of this country, it is logical that an organization such as the A. M. A. can profitably take stock of its expressed objectives or purposes, and its basic programs of service and activity. The work of this Committee has proved that American physicians can evaluate themselves professionally, and as citizens; can recognize areas of needed improvement; and can outline practical ways of maintaining the highest standards of health in this country, within the framework of private enterprise, the truly American way of life.

In a sincere desire to stimulate progress in medicine in every specialty and area, the A. M. A. has encouraged specialty societies, and it is only natural that in the multiplicity of medical groups the stature and prestige of the parent organization may not be so apparent. But it is easily possible for the A. M. A. to continue as the "fountainhead" of virile, worthwhile scientific groups, and yet sponsor such a bold, vigorous, constructive, logical program that its leadership will be recognized and respected more than ever before.

Clearly the members of the A. M. A. are convinced that sociological and economic trends and conditions of today constitute an important aspect in the medical care of the patient and of the practice of medicine.

Your reference committee recommends that the first recommendation of this special committee—that the House of Delegates consider amendment of Article II of the Constitution by this substitution: "The objectives of the Association are to promote the science and art of medicine and the betterment of public health and an understanding of the socioeconomic conditions which will facilitate the attainment of these objectives"—be referred to the Council on Constitution and Bylaws.

Your reference committee recommends that the Board of Trustees establish a mechanism which will assume the responsibility for promoting active liaison with each national medical society. The intent of this liaison should be to explore all fields of interrelationship between the A. M. A. and the national medical societies. There should be an attempt to define the area of activity of each organization. In the scientific fields the role of the A. M. A. might be primarily that of leadership, but every endeavor should be made to bring about coordination of the special fields of scientific interest of the other national medical organizations.

Since the Board of Trustees in Supplementary Report L has announced a very comprehensive plan to establish and develop a Division of Socio-Economic Activities, your reference committee feels that there is no necessity for the creation of a new council or committee on socioeconomics. The House of Delegates will be informed periodically on the progress of this new Division of Socio-Economic Activities through the medium of semiannual reports to the House and the regular media of publications.

Your reference committee approves the recommendation that the Board of Trustees give serious consideration to opening the publications of the Association to a free and open discussion of socioeconomic problems applicable to medicine. Members and officers of the Association should be encouraged to contribute items to this section of the publication or publications.

The Committee to Study A. M. A. Objectives and Basic Programs has served faithfully and correctly points out that the assignment given to it by this House last December was so comprehensive that no one group could be expected to cover the responsibilities completely, particularly in the space of a few months.

Since it is apparent to your reference committee that the work of analysis and improvement of basic programs of the A. M. A. will continue through the mechanisms mentioned in this report, this special committee should be relieved of further responsibility and we so recommend, with the additional recommendation of an expression by this House of Delegates of deep appreciation and thanks for a task well done. Special thanks are also due Dr. Frank G. Dickinson and his staff of the Bureau of Medical Economic Research for the tremendous service rendered in preparing this report. We urge every delegate to study his copy of the report very carefully and urge every physician to review with interest the printed summary and other comments in THE JOURNAL.

G. B. WILDER, M.D., Indiana
C. F. STROSNIDER, M.D., North Carolina
P. P. THOMPSON, M.D., Maine
W. F. COSTELLO, M.D., New Jersey
J. B. COPELAND, M.D., *Chairman,* Texas

MEDICAL NEWS

COLORADO

Dr. von Kaulla Participates in Broadcast.—Dr. Kurt N. von Kaulla, a member of the University of Colorado School of Medicine faculty, recently participated in a discussion which was recorded for broadcast throughout Europe by the Voice of America. He is one of four German-speaking researchers invited by the U. S. State Department to take part in the recorded discussion during a symposium on blood conducted at Wayne State University, Detroit. The 15-minute transcribed discussion concerned, among other subjects, progress made in America in dissolving blood clots. On the panel with Dr. von Kaulla were three research scientists visiting in the U. S., and representing Germany, Austria, and the Netherlands.

ILLINOIS

Meeting of Anesthesiologists.—The Illinois Society of Anesthesiologists will convene March 21 at the Lin [illegible] Beach Hotel, Chicago, with dinner at 7 p. m. and the scientific program beginning at 8 p. m. "The Limitations of Anesthesia in Poor Risk Patients" will be given by Dr. James E. Eckenhoff, professor of anesthesiology, University of Pennsylvania, Philadelphia. Reservations for dinner ($5.30) must be made not later than March 14. For information and reservation write Dr. Frank M. Grem, 546 N. Elmwood Ave., Oak Park, Ill.

Engineers Aid Medical Research.—Thirty-five Illinois Bell Telephone Company engineers have volunteered their know-how to help medical research in fighting cancer, heart disease, and infant deaths. New instruments resulting from their spare-time efforts were demonstrated Feb. 5 for the first time at the University of Chicago. The volunteers belong to an organization called SAVE—Service Activities of Volunteer Engineers. They have reported that accomplishments of the first year of work included:

1. Completion of working models of a three-ounce device to count the human heartbeat while being worn during a full day of normal activity.
2. Virtual completion of a training machine to teach laboratory technicians to identify cancer cells under the microscope.
3. Progress toward an electronic computer that instantaneously reports changes in the volume of air in the lungs of a baby in the hope of detecting hyaline membrane disease.
4. Progress toward an electronic circuit 10 times more sensitive than existing equipment to radiation from radioisotopes trapped in brain tumors.
5. Under development is an electronic calorimeter, which is a cumulative recording device to measure changes in body heat. Such an instrument would aid in studies of metabolism.

Another device is an electronic stethoscope. The idea for SAVE originated with William V. Kahler, president of Illinois Bell and a trustee of the University of Chicago. After consulting with physicians at the University of Chicago Clinics, the engineers set to work in basements, garages, and workshops at their homes in 20 suburbs and throughout Chicago. All the instruments developed through the efforts of SAVE reportedly will be put at the disposal of the medical profession. An enlarged report on SAVE will appear in the Medicine at Work section of THE JOURNAL, issue of March 21.

Chicago

Dr. Cooper Honored.—Dr. John A. D. Cooper, professor of biochemistry and assistant dean of Northwestern University Medical School, recently was honored by the University of Brazil when it conferred on him the degree of Doutor Honoris Causa, "in recognition of the work done in helping to establish and equip a radioisotope laboratory in the Institute of Biophysics at the university's medical school."

Annual Medical History Lecture.—The annual D. J. Davis Memorial Lecture on Medical History will be given at 1 p. m., Wednesday, April 22, in Room 221 of the Dental–Medical–Pharmacy Building of the University of Illinois, 1853 W. Polk St. The lecturer will be Dr. Lloyd G. Stevenson, professor of the history of medicine and dean of the Faculty of Medicine, McGill University, Montreal P. Q., Canada. His subject will be "The Early Development of Internal Medicine in the United States."

Lectures in Research in Cancer.—The last two lectures in the University of Chicago 1959 Winter Quarter series on Research in Cancer are arranged as follows: March 9, 5 p. m., "The Contribution of Experimental Gliomas to Human Disease," Dr. Harry M. Zimmerman, chief, Laboratory Division, Montefiore Hospital, New York City; March 16, 5 p. m., "Viral Etiology of Mouse Leukemia: Its Possible Implications for the Problem of Cancer," Dr. Ludwik Gross, chief, Cancer Research Unit, VA Hospital, Bronx, N. Y.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Hospital News.—Michael Reese Hospital and Medical Center has announced the appointment of Dr. Morris Weiss to the position of first Medical Director of Mandel Clinic, the Hospital's out-patient division. In this new position, Dr. Weiss, who was assistant professor of medicine, Baylor University College of Medicine, Waco, Texas, from 1956 to 1957, will be responsible for all medical care and education given at the clinic.

KANSAS

Centennial for State Society.—On Feb. 10 the charter issued by the Territorial Legislature of Kansas was 100 years of age and the Kansas Medical Society which was given "perpetual succession forever" survived its first century. The centennial is to be commemorated until the close of the annual session to be held in Topeka, May 4-6. A special program based on a frontier theme necessitates that the meeting be held at the Fairgrounds. Many events for public participation have been planned. A Hall of Health with educational exhibits for the public will be open for two weeks prior to the annual session. A book, "A Century of Medicine in Kansas," has been written with the cooperation of the Committee on History. The National Rural Health Conference at Wichita March 5-7, is also a part of the society's centennial celebration.

MAINE

Conference on Mental Retardation.—The first International Medical Conference on Mental Retardation, organized by the Maine Chapter of the American Academy of Pediatrics, the Division of Maternal and Child Health, Maine Department of Health and Welfare, and the Pineland Hospital and Training School, Pownal, will be held July 27-31 at the Eastland Hotel, Portland. The program will include in its five days of general sessions addresses on brain anatomy, the reticular system, head anomalies, phenylketonuria, lipoids, birth injury, embryology, infections, mongolism, erythroblastosis, therapy, psychiatry, psychology, and behavior disorders, by "outstanding authorities" on these subjects. Not intended to answer all questions on the problems concerning mental retardation but rather to construct the problems which have to be attacked scientifically, the conference is open to all physicians throughout the United States, Canada, and other countries, following immediately after the International Pediatric Congress at Montreal, Canada. For information write Dr. Ella Langer, State of Maine, Department of Health and Welfare, Augusta, Maine, Chairman, Arrangements Committee.

MARYLAND

Hygiene Lecture.—As part of the De Lamar Lectures in Hygiene of the School of Hygiene and Public Health, The Johns Hopkins University, Baltimore, a public lecture on "The Long Range Effects of Ionizing Radiations on the Individual" was presented by Dr. William R. S. Doll, lecturer in medical statistics and epidemiology, London School of Hygiene and Tropical Medicine, England, Feb. 20.

MASSACHUSETTS

Medical History Meeting.—The next meeting of the Benjamin Waterhouse Medical History Society will be a combined meeting with the Providence Medical Historical Society to be held at the Massachusetts Memorial Hospital, Monday, March 16. Dr. Seebert J. Goldowsky, director, Peripheral Vascular Clinic, Rhode Island Hospital, will be the speaker, presenting, "The Hospital at Portsmouth Grove." For information and reservations write Dr. John J. Byrne, 818 Harrison Ave., Boston 18, Secretary (KE 6-8600).

Dr. Bandler Named Department Chairman.—Dr. Bernard Bandler, of Cambridge, president-elect of the American Psychoanalytic Association, has been named chairman of the department of psychiatry at the Boston University School of Medicine. He has also been named psychiatrist-in-chief of the Massachusetts Memorial Hospitals. He has been associated with the school and with the hospital since 1947. Dr. Bandler is currently chairman of the Ad Hoc Committee on Education in Public Hospitals of the American Psychiatric Association in liaison with the American Psychoanalytic Association, a member of the executive committee of the American Psychoanalytic Association, training analyst for the Boston Psychoanalytic Society and Institute, Inc., and a member of the Medical Advisory Committee of Boston University's Sargent College.

MICHIGAN

Sight Testing for Children.—The eyesight of 325,837 Michigan school children was screened in 1958 by technicians employed by local health departments and local schools, the Michigan Department of Health has reported. Each child was screened for nearsightedness, farsightedness, astigmatism, and muscle imbalance. Of the children screened, 37,035 (11.5%) were referred to doctors to have an eye examination for the first time. During 1958, 57 children were added to the state health department's Register of Children with Severe Visual Handicaps. Nine hundred and thirty-nine youngsters are now registered, 187 whom are of preschool age.

MISSOURI

Dr. Sante Receives Radiology Award.—Dr. LeRoy Sante, professor of radiology and director of the department, Saint Louis University School of

Medicine, received a gold medal award from the American College of Radiology at ceremonies in Chicago Feb. 6, during the college's annual convocation. Dr. Sante was one of three radiologists throughout the country unanimously chosen for the award by the board of chancellors of the college. The gold medal award is presented annually "for distinguished and extraordinary service to the American College of Radiology and to the profession for which it stands." The award also will be presented posthumously to Dr. C. Edgar Virden, formerly chief of the radiologic service at St. Joseph's Hospital, Kansas City, Mo., and to Dr. Robert S. Stone, director of the department of radiology, University of California.

MONTANA

Joint Meeting in Missoula.—The Montana Heart Association and the Montana Trudeau Society will sponsor a joint meeting in Missoula, April 17-18. All sessions will convene at the Florence Hotel and all physicians and interested lay people are invited. The speakers at this meeting will include Dr. Herbert E. Griswold, chairman, department of cardiology, University of Oregon Medical School, Portland; Dr. Richard E. Fowler, professor of pediatrics, Tulane University School of Medicine, New Orleans; Dr. Walter M. Kirkendall, clinical associate professor of internal medicine, State University of Iowa College of Medicine, Iowa City; Dr. David T. Smith, professor of bacteriology and associate professor of medicine, Duke University School of Medicine, Durham, N. C.; Dr. Jay A. Myers, professor of internal medicine, University of Minnesota Medical School, Minneapolis; and Dr. Carroll J. Martin, Seattle Sanitarium.

NEW JERSEY

Dr. Stevenson Named Department Chairman.—Dr. Stuart S. Stevenson was appointed professor and chairman of the department of pediatrics, Seton Hall College of Medicine, Jersey City. Dr. Stevenson, whose appointment was effective March 1, comes to Seton Hall from the University of Pittsburgh School of Medicine, where he has been acting chairman of the department of pediatrics. In addition, he was acting medical director and chief of staff at the Children's Hospital in Pittsburgh. He is chairman of the Committee on Residency Fellowships of the American Academy of Pediatrics.

NEW YORK

Dr. Weinberg to Lecture on Hypnosis.—The New York County Chapter of the American Academy of General Practice will present Dr. Abraham Weinberg, chairman, Committee on Mental Hygiene, New York Academy of General Practice, and lecturer in medical hypnosis, Seton Hall College of Medicine, March 12, 9 p. m., room 65 at the Academy of Medicine, 2 E. 103rd St., New York City. Dr. Weinberg will discuss "Indications and Techniques of Hypnosis for the General Practitioner." For information write Dr. Stanley H. Greenwald, 325 E. 79th St., New York 21, Secretary.

Personal.—The provisional appointment of Dr. Ray K. Brown as associate director of the State Health Department's Division of Laboratories and Research effective Jan. 29, has been announced by Dr. Herman E. Hilleboe, state health commissioner. Dr. Brown has served since 1953 as assistant director of the department's Laboratories for Biochemistry and Immunology.——Dr. James W. Bartlett Jr. has been named assistant dean of the University of Rochester School of Medicine and Dentistry. He is in charge of admissions and will assist in administration of scholarships and loans. Dr. Bartlett is an instructor in the department of psychiatry.

OHIO

Dr. Dods to Give Rachford Lectures.—The 27th annual series of the Benjamin Knox Rachford lectureships will take place in Cincinnati April 21 and 22, at 8:30 p. m. Dr. Lorimer F. Dods, professor of child health at the University of Sydney, Australia, will deliver these lectures in the auditorium of the Children's Hospital Clinic and Research Building. On April 21 Dr. Dods will lecture on "Pædiatrics in the Antipodes," and on April 22 his subject will be "Some Pædiatric Philosophy."

PENNSYLVANIA

Bicentennial Week in Pittsburgh.—The Pittsburgh Bicentennial Lecture Week in Medicine was held during the last week in February. Four lectures were presented in the University of Pittsburgh Schools of the Health Professions auditorium. Guest lecturers were Theodore T. Puck, Ph.D., chairman, department of biophysics, University of Colorado School of Medicine, Denver; Dr. George W. Thorn, Hersey professor of theory and practice of physic, Harvard Medical School, Boston; Dr. Carl V. Moore, chairman, department of medicine, Washington University School of Medicine, St. Louis; Dr. Charles W. Mayo, head, surgery section, Mayo Clinic, Rochester, Minn.

Philadelphia

Annual Lecture.—The Kappa Pi Chapter of the Phi Delta Epsilon Fraternity will hold its annual Bernard Comroe lectureship series March 20 in the Medical Alumni Hall of the Hospital of the University of Pennsylvania. The guest speaker will be Dr. Harold G. Wolff, professor of medicine (neurology), Cornell University Medical College, New York City. His subject will be "Headache."

Dr. Koprowski Receives French Award.—Dr. Hilary Koprowski, director of the Wistar Institute of Anatomy and Biology and president of The New York Academy of Sciences, received the cross of a commander of the Ordre du Merite pour la Recherche et l'Invention from the Societe d'Encouragement pour la Recherche et l'Invention (French) at a ceremony in the Wistar Institute museum Feb. 11. The Societe d'Encouragement pour la Recherche et l'Invention was formed in 1901 under the sponsorship of the French government ministries of education, public health, and industry and commerce. A committee composed of authorities in the various fields of science chooses a few researchers and inventors of high standing each year for awards of various degrees in the society's Ordre du Merite. Dr. Koprowski is chairman of the Inter-American Society of Microbiologists and a member of the virology and rickettsiology study section of the National Institutes of Health.

TEXAS

Steel Company Donates Community Hospital.—Hospital in the Pines, a 30-bed hospital costing more than 30 million dollars and built by the Lone Star Steel Company, was turned over to the people at a formal dedication ceremony recently. The president of the company, Mr. E. B. Germany, presented the title to the board of directors. The gift of the hospital was noncommittal, and the Steel Company will have no voice in the hospital management. The board of seven members will be entirely independent of the company. Mr. Thomas K. Ewan, chairman of the board, accepted the hospital in behalf of the board at the ceremony. In the spring of 1956 Lone Star Steel employed an independent firm of hospital consultants to determine the site that would best serve the area. Local civic and business leaders organized Hospital in the Pines, Inc. and the charter was granted in 1957. The design will permit later expansion. Dr. Lowell E. Rutledge, of Daingerfield, is chief of staff.

GENERAL

Fellowships in Forensic Pathology.—Under the auspices of the College of American Pathologists, there is a vacancy for a fellow in forensic pathology for a period of six months' training at the Armed Forces Institute of Pathology. Stipend is $2,500. Six months' credit toward the Subspecialty Certificate in Forensic Pathology given by the American Board of Pathology will be allowed to the individual filling this fellowship. Interested individuals may apply to the AFIP or to Dr. Russell S. Fisher, Chairman, Committee on Forensic Pathology, College of American Pathologists, Prudential Plaza, Chicago.

Fraternity Meeting in Miami Beach.—The seventh annual interim scientific meeting of Phi Lambda Kappa, national medical fraternity, will be held at the Deauville Hotel, Miami Beach, Fla., April 5-12. The five-day program, starting Monday, April 6, will be for the benefit of the general practitioner and will feature papers and symposiums by specialists in their fields. All members of the medical and dental professions are welcome. For registration and information, write Dr. Samuel L. Lemel, 1621 Euclid Ave., Cleveland 14.

Tri-State Association Meets in Winston-Salem.—The annual meeting of the Tri-State Medical Association for Virginia, North Carolina, and South Carolina will be held March 16-17 in Winston-Salem, N. C. Five panel discussions are arranged: "Gastroenterology," "Dermatology," "Psychiatry," "Cardiac," and "Trauma." The following papers will be presented:

Urology—A New Surgical Approach for the Correction of Urinary Incontinence, Dr. L. T. Pennington, Greensboro, N. C.
Infertility, Dr. John Monroe, Winston-Salem, N. C.
Hypnosis in Pregnancy, Dr. T. W. Littlejohn, Durham, N. C.
Radiation Hazards, Dr. I. Meschan, Winston-Salem, N. C.

Guest speaker at the banquet at 7 p. m., March 16, will be Dr. Robert F. Clodfelter, of Winston-Salem.

Meeting on Anesthesia Research in Miami Beach.—The 33rd congress of the International Anesthesia Research Society will be held April 20-23 in Miami Beach, Fla. Papers to be presented by foreign participants include the following:

Anesthesia for the Ambulant Surgical Patient, Dr. Eric Webb, Vancouver, British Columbia, Canada.
A Method of Anaesthesia for Per-Oral Endoscopy, Dr. J. D. A. Firth, Montreal, Quebec, Canada.
Anesthetic Techniques for Tonsillectomy and Adenoidectomy in Children, Dr. Oscar V. Ribeiro, Rio de Janeiro, Brazil.

Three panel discussions are planned: "Open Cardiac Surgery," "Recurrent Staphylococcal Infections in Modern Hospitals," and "Pharmacology." Two movies are scheduled, and discussions will conclude each session.

Aero Medical Meeting in Los Angeles.—The 30th annual meeting of the Aero Medical Association will be held April 27-29 at the Statler Hilton Hotel, Los Angeles. Brig. Gen. M. S. White, M. C., USAF, president of the association, will open the program with an address, followed by the Louis H. Bauer Lecture, presented by Dr. Hans Selye, Faculty of Medicine, University of Montreal, on "Stress in Aviation Medicine." Two symposiums are planned: "Aeromedical Aspects of Stress," with Dr. Selye as chairman, and "Toxicological Health Hazards," with Col. Harold V. Ellingson, M. C., USAF, director of education and plans, USAF School of Aviation Medicine, Randolph Air Force Base, Texas, as chairman. The program will include speakers from Canada, England, Italy, France, Germany, and Norway. For information write Dr. T. H. Sutherland, P. O. Box 26, Marion, Ohio, Secretary.

Southwestern Meeting on Nuclear Medicine.—The fourth annual meeting of the Southwestern Society of Nuclear Medicine will be held in the Roosevelt Hotel, New Orleans, March 14-15, under the presidency of Dr. Herbert C. Allen Jr., Houston, Texas. The program includes 17 scheduled papers and three panel discussions with the following titles and moderators:

Some Aspects of Isotope Use in Studies of Electrolyte Metabolism, Dr. Sam A. Threefoot, New Orleans, La.
Medical Management in Radiation Accident Cases, John Hidalgo, M.S., New Orleans, La.
Symposium on Scintillation Scanning, Dr. Herbert C. Allen Jr., Houston, Texas.

The business meeting and dinner are planned for the evening of March 14. For information write Dr. Samuel B. Nadler, 1520 Louisiana Ave., New Orleans 15, chairman of the program committee.

Proctology Meeting in New York City.—The 11th annual convention of the International Academy of Proctology will be held at The Plaza, New York City, April 5-9. The international, national, and local program committees are planning a seminar on practical techniques for office and hospital. There will be special emphasis on anal and rectal panel presentations, and on newer treatment methods, as requested by those who attended the Mexico City meeting in 1958. Motion-picture demonstrations are planned. Members and nonmembers of the academy and their wives are invited to the banquet April 8. The Women's Auxiliary has planned a program for the wives and their guests. There is no fee for attendance at these teaching sessions of the academy. For information, write the International Academy of Proctology, 147-41 Sanford Ave., Flushing, N. Y., Dr. Alfred J. Cantor, Executive Secretary.

Allergists Meeting in San Francisco.—The 15th congress of the American College of Allergy will be held March 15-20 at the Mark Hopkins Hotel, San Francisco. A graduate instructional course in allergy will be conducted March 15-17. Dr. Merle W. Moore, president of the college, will speak at the general session March 18. On March 19 a panel discussion, "Repository Injection Treatment of Inhalant Allergy," will be moderated by Dr. Lawrence J. Halpin. Dr. Max Samter, president, American Academy of Allergy, will present "Semantics—and the Future of Allergy" the afternoon of March 19. Sectional sessions will be conducted March 20 under the following headings: Dermatologic Allergy, Psychosomatic Medicine, Technology, and Pediatric Allergy. Tours, movie sessions, and exhibits are planned. For information write the American College of Allergy, 2049 Broadway, Boulder, Colo.

Triological Society Meeting in Hot Springs, Virginia.—The American Laryngological, Rhinological, and Otological Society, Inc., "The Triological Society," will meet March 10-12 at the Homestead, Hot Springs, Va. A business meeting will precede each session. The presidential address will be given by Dr. Gordon D. Hoople, Syracuse, New York. Speakers on the program are as follows: Drs. George F. Reed, Boston; John J. O'Keefe, Philadelphia; Robert E. Boswell, Dayton, Ohio; John F. Daly and Samuel Rosen, New York City; Walter E. Heck, Robert C. McNaught, Leonard G. Dobson, and Francis S. Greenspan, San Francisco, Calif.; Victor R. Alfaro, Washington, D. C.; George E. Shambaugh Jr. and Henry B. Perlman, Chicago; Lester A. Brown, Atlanta, Ga.; Miles L. Lewis Jr., New Orleans; Bruce Proctor, Detroit; Maurice Schiff, Oakland, Calif.; Clair M. Kos, Iowa City; and Howard P. House, Los Angeles. For information write C. Stewart Nash, 708 Medical Arts Building, Rochester 7, New York, Secretary.

Nigerian Physician Wins Rehabilitation Award.—The appointment of Dr. Badejo O. Adebonojo of Nigeria as the recipient of the "Betsey Barton Fellowship" in Rehabilitation of the World Rehabilitation Fund has been announced by the fund's president, Dr. Howard A. Rusk. The "Betsey Barton Fellow" in rehabilitation, to provide advanced training in rehabilitation in the United States for a physician from Africa or Asia, was made possible by a grant to the World Rehabilitation Fund from the Aaron E. Norman Fund, Inc. The fellowship was named in honor of Miss Betsey Barton "because of her leadership in extending and expanding rehabilitation services throughout the world." Miss Barton, who is a paraplegic, is a member of the Board of Directors of the National Paraplegia Foundation, Inc., and of the board of Trustees of the Institute for the Crippled and Disabled. Dr. Adebonojo will begin his advanced training March 1 at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York City. The World Rehabilitation Fund, Inc., is a nonprofit organization supported by American industry, foundations, and individuals to assist in the international development of rehabilitation services for the physically handicapped.

Annual Southern Conference on Gerontology.—"Society and the Health of Older People" will be the theme of the ninth annual Southern Conference on Gerontology, to be held on the campus of the University of Florida, Gainesville, March 19-20. The program will deal primarily with "psychosocial aspects of wellness and illness." Sessions will be devoted to the challenge of optimum health in old age; anthropological, sociological, and psychological aspects of health; social factors in the health of the elderly as seen from the standpoint of the physician, the social worker, the nurse, and the biologist; and public and professional aspects of the health care of the aged. Participants include Dr. Halbert L. Dunn, chief, National Office of Vital Statistics; Marion T. Loftin, Ph.D., of Mississippi State College; Ethel Shanas, Ph.D., of the University of Chicago; Robert W. Kleemeier, Ph.D., of Washington University (St. Louis); Carter C. Osterbind, Ph.D., of the University of Florida; Dr. Samuel Gertman, of the University of Miami; and Dr. Albert V. Hardy, of the Florida State Board of Health. For information write Irving L. Webber, Ph.D., Institute of Gerontology, Peabody Hall, University of Florida, Gainesville, or Robert L. Fairing, Ph.D., General Extension Division, Gainesville. The meetings are sponsored by the Institute and the General Extension Division of Florida.

Youth Fitness Week.—A Presidential Proclamation designating May 3-9, 1959, as National Youth Fitness Week, reads as follows:

WHEREAS the ongoing strength of our Nation depends upon health of our young people; and

WHEREAS we must always strive to improve the fitness of our youth by determined and coordinated efforts; and

WHEREAS, in this challenging world, it is essential that our young people recognize their obligation to themselves, to their families, and to the Nation, to endeavor to keep themselves mentally, emotionally, spiritually, socially, and physically fit; and

WHEREAS the President's Council on Youth Fitness has recommended that a National Youth Fitness Week be designated:

NOW, THEREFORE, I, DWIGHT D. EISENHOWER, President of the United States of America, do hereby proclaim the week beginning May 3, 1959, as National Youth Fitness Week.

I request officials of the Government, and I urge parents, young people, and interested local and national organizations, to use all appropriate means during that week to promote programs and activities demonstrating the importance of youth fitness to the end that we may assure the continuing strength and wellbeing of our people.

In Witness Whereof, I have hereunto set my hand and caused the Seal of the United States of America to be affixed.

Done at the City of Washington this thirty-first day of January in the year of our Lord nineteen hundred and fifty-nine and of the Independence of the United States of America the one hundred and eighty-third.

Dwight D. Eisenhower

Report on Age and Mortality.—Despite the marked progress made in reducing mortality in the United States, 40% of all deaths still occur at ages under 65, according to statisticians of the Metropolitan Life Insurance Company. More than 670,000 deaths a year are at ages under 65. Included were about 108,000 babies less than a year old and more than 400,000 people in the 45-64 year age bracket. Most deaths among infants are associated with pathological conditions existing prior to birth or with the hazards of the birth process, the statisticians point out. Three-fifths of the mortality results from "diseases of early infancy," a category comprising mainly deaths attributed to premature birth, postnatal asphyxia, and injuries at birth. Congenital malformation accounts for an additional 14% of infant deaths. In the mortality for the 1-24 age group, accidents are responsible for a greater number of deaths than all other causes combined, even among the girls. Among boys at these ages, motor vehicle accidents alone account for more than one-quarter of the deaths. In the 25-44 age group, the diseases of the heart, arteries, and kidneys account for nearly a third of the deaths among the males, with accidents a close second. Among women at these ages, cancer heads the list of causes of death. At ages 55-64 diseases of the heart, arteries, and kidneys account for nearly three-fifths of the deaths among men and for more than half the total among women. Second in rank is cancer, which accounts for 20% of the deaths among men and nearly 30% among women.

Education Foundation Has Record Campaign.—The 1958 campaign for the American Medical Education Foundation resulted in a record total of $1,120,044 plus interest, according to John W. Hedback, executive secretary of the Foundation. State and county AMEF committees raised the amount from physicians during the year. The grants to 85 medical schools were made at the 55th annual Congress on Medical Education and Licensure in Chicago, Feb. 7-10. The 1958 fund represents a 15% increase over 1957 totals. Thirty-five states reported increases, ranging from $9.06 (Nebraska) to $31,000 (New Jersey). The total dollar increase amounted to $148,000. Indiana, after one year as a dues-increase state, reported $30,600, for a total two and a half times that of a year ago. Alaska jumped from $125 in 1957 to $1,414.50 in 1958—an increase of 1,131%. Other spectacular climbs were made by Idaho (342%) and South Carolina (281%). Illinois physicians contributed $200,191, placing them first in the nation. California followed with $171,611. Both are dues-increase states. Arizona's 1958 total of $12,600 includes $1,000 from retail druggists. The amount stems from a program initiated late in the year through which druggists send gifts to AMEF in physicians' names in lieu of Christmas gifts. The plan was endorsed by the Arizona Retail Druggists Association. The Woman's Auxiliary to A. M. A. established a new record themselves with contributions of $126,200. Delaware, Maryland, Massachusetts, New York, Ohio, Texas, and Washington, D. C., all reported sizeable increases over 1957—ranging from $2,350 to $14,300 for an average of $6,000.

Contest for Paper on Gastroenterology Research.—The American College of Gastroenterology has announced the establishment of an award contest for the best unpublished paper on research in gastroenterology or an allied field. This award is to be known as the Henry G. Rudner Sr. Award, honoring Dr. Henry G. Rudner Sr., of Memphis, Tenn., chairman of the Research Committee of the American College of Gastroenterology and former chairman of the board of governors of the organization. This contest will be open to all those possessing the degree of doctor of medicine from a recognized medical school or university. All papers submitted must represent original work in gastroenterology, or an allied field, and must not have been previously published except for abstracts or short preliminary reports. It must not have been previously presented on the program of any scientific meeting. The papers may be on clinical or basic science; clinical papers must not be case records, but controlled clinical work. The length of a paper is no criterion for originality or value. All entries for the 1959 award must be typewritten in English, double-spaced on one side of the paper, and submitted in six copies. The award will be made at the annual convention banquet of the college, in Los Angeles, in September, 1959. The prize will be an award of $750 plus an additional $250 for traveling expenses. The paper selected for an award becomes the property of the American College of Gastroenterology and the decision of the judges will be final. All entries must be received no later than June 1 and should be addressed to: The Research Committee, American College of Gastroenterology, 33 W. 60th St., New York 23.

Committee on Bioastronautics.—The National Academy of Sciences–National Research Council announced the organization of the Armed Forces–National Research Council Committee on Bio-Astronautics. The committee will advise the Armed Forces, on their request, in any matter concerning the biological or medical aspects of space exploration. Policy decisions and the programming of activities within the committee will be the responsibility of an executive council to which the following scientists have been appointed by Dr. Detlev W. Bronk, president of the Academy–Research Council: chairman, Otto H. Schmitt, Ph.D., department of physics, University of Minnesota; vice-chairman, Melvin Calvin, Ph.D., department of chemistry, University of California, Berkeley; Howard J. Curtis, Ph.D., department of biology, Brookhaven National Laboratory; Paul M. Fitts, Ph.D., department of psychology, University of Michigan; Brig. Gen. Donald D. Flickinger, directorate of life sciences, Air Research and Development Command; Dr. John D. French, department of anatomy, University of California Medical Center, Los Angeles; Capt. Charles F. Gell, Office of Naval Research; James D. Hardy, Ph.D., U. S. Naval Air Development Center, Johnsville, Pa.; and Col. Robert H. Holmes, Research and Development Command, Office of the Surgeon General, Department of the Army. The full Committee on Bio-Astronautics—which will consist of more than 100 members, of whom at least half will be nominees of the Armed Forces—will serve as a conference or forum of active investigators, meeting periodically to review scientific and technical problems, exchange information, and establish liaison between investigators with allied interests. Administrative responsibility for the committee has been vested within the Academy–Research Council's Division of Medical Sciences, whose chairman is R. Keith Cannan, ScD. Acting executive secretary to the committee is Dr. Sam F. Seeley.

Directory of Blood Facilities.—A directory and description of blood facilities and services has been released by the Joint Blood Council, a nonprofit national organization with headquarters in Washington, D. C. It shows the location of facilities, the extent of their operations, how they are organized, what specific services they offer, and other information of importance to physicians, hospitals, and any person or organization interested in blood and its derivatives. The directory is based on data obtained from a questionnaire sent to all known blood banks, hospitals, and clinics that offer blood-handling services. The questionnaire was sent to 3,150 institutions and 2,202 replied. Those that failed to return the information will have an opportunity to supply it for future directories. The directory will be distributed free by the council to all institutions and organizations that participated in its preparation, according to Dr. Frank E. Wilson, executive vice-president. Others may obtain it at the cost price of $1.50 each from the Joint Blood Council headquarters, 1832 M Street, N. W., Washington 6, D. C. The council was formed three years ago by the American Association of Blood Banks, the American Hospital Association, the American Medical Association, the American National Red Cross, and the American Society of Clinical Pathologists "to establish a national blood program in order to assure an adequate supply of blood and blood derivatives to the civilian and military population at all times of peace or emergency and to take all appropriate action in connection therewith." Information includes the following: (1) Of the facilities listed, 1,832 administer whole blood. Also, 1,287 administer plasma, 1,021 serum albumin, 994 packed red blood cells, and 311 platelets, with many of the facilities engaging in a number of these activities. (2) Artery banks are maintained by 116, eye banks by 36, bone banks by 200, skin banks by 24, and mother's milk banks by 20. (3) A total of 1,325 blood banks store whole blood, record donor histories, and have as their primary purpose the recruitment of donors and complete laboratory blood processing. (4) Two out of every three organizations listed have no reciprocity system for the exchange or resupply of blood. Of the remaining one-third, 470 use the American Red Cross system, 240 that of the American Association of Blood Banks, and 110 use both systems. Dr. Leonard W. Larson is president of the Joint Blood Council.

FOREIGN

International Course on Tomography.—The fourth International Course on Tomography will be held at the Radiology Institute, University of Genoa, Italy, under the direction of Prof. Alessandro Vallebona. This course will last eight days and deal particularly with the recent progresses in tomographical methods. The period September-October, 1959 has been chosen for this meeting. All lectures, while read in the original language, shall be contemporarily translated into Italian, French, English, German, and Spanish. All interested physicians are advised to write Prof. Neopolo Macarini, General Secretary, Instituto di Radiologia della Universita-Ospedale San Martino, Genova, Italia, for information.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: Stations around the world, Feb. 17. Deadline for foreign applications was Nov. 17. The following examination will be held Sept. 22 with application deadline of June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arkansas:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

Connecticut:* *Regular. Examination.* Hartford, March 10-12. Acting Sec., Dr. Stanley B. Weld, 160 St. Ronan St., New Haven.

Florida:* *Examination.* Miami Beach, June 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, June. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Michigan:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minnesota:* *Reciprocity.* St. Paul, February. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul.

Montana: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination.* Trenton, June 16-19. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

New Mexico:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

North Carolina: *Examination.* June Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

Oklahoma:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon:* *Written.* Portland, Apr. 17-19. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

South Carolina: *Reciprocity.* Columbia, May 12; *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

Texas:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination.* Salt Lake City, July 8-10. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Virginia: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

Wisconsin:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Madison, April 17 and Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, June 1. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

District of Columbia: *Examination.* Washington, May 18-19. Address: Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.

Florida: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Iowa: *Examination.* Des Moines, April 14. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

Kansas: *Examination.* Kansas City, June. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, May 8-9. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Nebraska: *Examination.* Omaha, May 5-6. Director, Mr. R. K. Kirkman, Bureau of Examining Boards, 1009 State Capitol Bldg., Lincoln.

Oklahoma: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon: *Written.* Mar. 7. Sec., Dr. Earl M. Pallett, Box 5175, Eugene.

Tennessee: *Examination.* Memphis, Mar. 25-26. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

Texas: *Examination.* Austin, Galveston, Houston, Apr. 17-18. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, April 4. Final date for filing application is March 27. Milwaukee, June 6. Final date for final application is May 29. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

DEATHS

Bietsch, Charles Frederick, Pittsburgh; University of Pittsburgh School of Medicine, 1913; specialist certified by the American Board of Obstetrics and Gynecology; an associate member of the American Medical Association; fellow of the American College of Surgeons; associated with the Mercy Hospital and the Roselia Foundling and Maternity Hospital; died Dec. 6, aged 71.

Brownell, William Flockton Ⓜ Fort Collins, Colo.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; past-president of the Larimer County Medical Society; veteran of World War I; on the staff of the Larimer County Hospital; died Dec. 5, aged 84.

Burpee, Benjamin Prescott, Manchester, N. H.; Harvard Medical School, Boston, 1914; veteran of World War I; president of the New Hampshire Board of Registration in Medicine; associated with the Elliot Hospital, where he died Nov. 27, aged 69.

Bushard, Bruce Lauren Ⓜ Lieut. Colonel, U. S. Army, Washington, D. C.; Northwestern University Medical School, Chicago, 1947; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; service member of the American Medical Association; veteran of World War II; entered the regular Army in 1948; died Dec. 10, aged 36.

Chisholm, Julian Ford Sr. Ⓜ Savannah, Ga.; University of Maryland School of Medicine, Baltimore, 1900; fellow of the American College of Surgeons; past-president of the Georgia Ophthalmological Club; member of the Seaboard Air Line Railway Surgeons Association; veteran of World War I; for more than 40 years oculist for the Seaboard and Central of Georgia Railways; on the staffs of the Telfair Hospital, Central of Georgia Railway Hospital, and St. Joseph's Hospital; died Dec. 13, aged 82.

Clark, Daniel Ennis, Parkersburg, W. Va.; University of Louisville (Ky.) School of Medicine, 1945; formerly a captain in the medical corps, Army of the United States; died Dec. 21, aged 42.

Clarke, Thomas Greene, Hyannis, Mass.; Tufts College Medical School, Boston, 1911; veteran of World War I; died in the Cape Cod Hospital Dec. 17, aged 70.

Cohen, Herman Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; died in the Morrisania Hospital Nov. 26, aged 77.

Cruikshank, Alexander Ⓜ Detroit; McGill University Faculty of Medicine, Montreal, Que., Canada, 1895; died Dec. 15, aged 87.

Cunningham, Robert Blythe Ⓜ Booneville, Miss.; Tulane University School of Medicine, New Orleans, 1926; fellow of the American College of Surgeons; veteran of World War I; vice-president of the Prentiss County Home Bank; member and past-president and secretary of the staff of the Northeast Mississippi Hospital, where he died Dec. 13, aged 61.

Cunningham, William Harry Ⓜ Rockford, Ill.; Chicago College of Medicine and Surgery, 1909; veteran of World War I; served on the staff of St. Anthony Hospital; died in Pittsburgh Dec. 1, aged 77.

Davidson, Alfred Ⓜ Chelsea, Mass.; Tufts College Medical School, Boston, 1910; also a graduate in pharmacy; on the staff of the Chelsea Memorial Hospital; died Dec. 14, aged 78.

Delzell, David Deronda Ⓜ Toledo, Ohio; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; on the staff of the Riverside Hospital; died Dec. 22, aged 73.

Dillard, James Bascom Ⓜ Davisboro, Ga.; Atlanta Medical College, 1894; also a graduate in pharmacy; served as president of the Washington County Medical Society; died Nov. 18, aged 86.

Dillon, John Alfred Jr. Ⓜ Austin, Texas; University of Kansas School of Medicine, Kansas City, 1935; service member of the American Medical Association; veteran of World War II; a lieutenant colonel and flight surgeon in the U. S. Air Force Reserve; died in the USAF Hospital at Lackland Air Force Base Nov. 18, aged 49.

Durrill, Everett Lee Ⓜ Pueblo, Colo.; Northwestern University Medical School, Chicago, 1931; fellow of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; on the staff of the Colorado State Hospital; died in Georgetown Dec. 3, aged 54.

Eakins, Olin Martin, Miami Beach, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1899; an associate member of the

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Ⓜ Indicates Member of the American Medical Association.

American Medical Association; member of the Medical Society of the State of Pennsylvania; formerly medical director of the Reliance Life Insurance Company in Pittsburgh; died Dec. 23, aged 84.

Frank, Louis James Ⓜ Huntington, N. Y.; Long Island College Hospital, Brooklyn, 1910; served on the faculty of his alma mater; physician in charge of the venereal disease clinic for the New York Health Department; on the staffs of the Long Island College Hospital, Brooklyn Women's Hospital, and Kings County Hospital, all in Brooklyn; specialist certified by the American Board of Dermatology and Syphilology; member of the Brooklyn Dermatological Society; died Oct. 12, aged 70.

Friedman, David Dudley, Brooklyn; Long Island College Hospital, Brooklyn, 1924; died Nov. 7, aged 59.

Frizell, William Henry Ⓜ Brookhaven, Miss.; University of Nashville (Tenn.) Medical Department, 1897; past-president of the Mississippi State Medical Association and served as president of its Fifty Year Club; past-president of the Tri-County–Pike–Lincoln–Copiah–Walthall Counties Medical Society, of which he was secretary for many years; a director of the Mississippi division of the American Cancer Society; for many years county health officer; member of the state board of health from 1930 to 1936; a director of the Mississippi Hospital Medical Service (Blue Cross–Blue Shield); died in the King's Daughters Hospital Dec. 3, aged 86.

Furgason, Allen P., Lincoln, Neb.; Northwestern Medical College, St. Joseph, Mo., 1889; an associate member of the American Medical Association; died in Phoenix, Ariz., Nov. 13, aged 91.

Giering, Herman J., Baltimore; Baltimore University School of Medicine, 1898; died in the Church Home and Hospital Nov. 25, aged 83.

Golden, William Colyn Ⓜ Clanton, Ala.; Louisiana State University School of Medicine, New Orleans, 1935; staff member and board member at the Chilton County Hospital; died in Birmingham (Ala.) Hospital Dec. 17, aged 51.

Hammond, Robert Lee Ⓜ Jackson, Ga.; University of Georgia Medical Department, Augusta, 1920; medical director of the Butts County Health Department; died Dec. 8, aged 64.

Hanson, William Clinton Ⓜ Augusta, Maine; Harvard Medical School, Boston, 1905; member of the Massachusetts Medical Society; veteran of World War I; formerly practiced in Belmont, Mass., where for 32 years he was school physician; served as assistant and acting secretary of the Massachusetts Department of Health; awarded a gold medal by the international jury of awards at the Panama-Pacific Exposition in Washington in 1915; died in Farmingdale Dec. 10, aged 83.

Hargis, Frank Cooper, Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1901; died in Columbia Nov. 4, aged 81.

Healy, Joseph Cornelius, Lockport, N. Y.; St. Louis University School of Medicine, 1924; health officer of Pendleton and Lockport; on the staffs of the Millard Fillmore Hospital in Buffalo and the Lockport Memorial Hospital; died Dec. 15, aged 59.

Henry, Martin Rudolph Ⓜ St. Peter, Minn.; University of Nebraska College of Medicine, Omaha, 1925; since 1941 on the staff of the St. Peter State Hospital; died suddenly Dec. 10, aged 58.

Herrington, Van Dolph Ⓜ Pryor, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1925; on the staff of the Grand Valley Hospital; member of the New Mexico Medical Society; died Dec. 2, aged 63.

Herron, Henry Harrison Ⓜ Jackson, Tenn.; University of Tennessee College of Medicine, Memphis, 1934; veteran of World War II; associated with the Webb–Williamson Hospital and the Jackson–Madison County General Hospital, where he died Dec. 6, aged 46.

Herron, Thomas Basil Ⓜ Monessen, Pa.; University of Pittsburgh School of Medicine, 1911; veteran of World War I; medical director of the Pittsburgh Steel Company; served as school director and president of the board; president of Peoples National Bank & Trust Company until its merger with Mellon Bank and Trust Company, when he became a director; associated with the Charleroi–Monessen Hospital in Charleroi, where he died Dec. 3, aged 69.

Hibbert, Russell William Jr. Ⓜ Greeley, Colo.; born in Hannibal, Mo., Jan. 30, 1916; St. Louis University School of Medicine, 1939; served on the faculty of the University of Colorado School of Medicine in Denver; member of the American Rheumatism Association; veteran of World War II; in 1958 president of the Weld County Cancer Society; once served as a physician for the Greeley High School football team; in January, 1949, the Greeley Junior Chamber of Commerce presented him with its annual award of outstanding young man of the year; honored for his contributions to the community and its youth; in 1953 received the Silver Beaver Award for his contribution to Boy Scouting; died Dec. 4, aged 42.

Hift, Robert Ⓜ Chicago; Medizinische Fakultät der Universität, Vienna, Austria, 1909; clinical associate in medicine at the Chicago Medical School; associated with American, McKenna, Weiss Memorial, Mount Sinai, and Forkash Memorial hospitals; died Dec. 22, aged 74.

Hodge, Benjamin Ervin, Wilmington, Del.; Johns Hopkins University School of Medicine, Baltimore, 1924; specialist certified by the American Board of Pediatrics; physician in charge in the general services department of the Du Pont Company; formerly on the staff of Johns Hopkins Hospital, Baltimore, where he died Nov. 28, aged 59.

Hoerr, Normand Louis, Cleveland; Graduate School of Medicine of the Division of the Biological Sciences, University of Chicago, 1931; on the faculty of the Western Reserve University School of Medicine; formerly on the faculty of his alma mater; died Dec. 14, aged 56.

Hole, Melvin Leo Ⓜ Danville, Ill.; Northwestern University Medical School, Chicago, 1911; fellow of the International College of Surgeons and the American College of Surgeons; member of the Industrial Medical Association; past-president of the Vermilion County Medical Society; veteran of World War I; on the staffs of Lake View and St. Elizabeth hospitals; died in Phoenix, Ariz., Dec. 12, aged 70.

Hollander, Beatrice Elsie Sterling Ⓜ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1941; died Dec. 11, aged 41.

Hooper, Lester E. Ⓜ Indianola, Iowa; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1908; veteran of World War I; in 1958 received the Simpson College Award for community service; died Dec. 6, aged 71.

Huckaby, William Ramsey Jr., Huntsville, Ala.; University of Tennessee College of Medicine, Memphis, 1956; interned at the Confederate Memorial Medical Center in Shreveport, La., and served a residency at the City of Memphis Hospitals in Memphis; died Dec. 9, aged 28.

Huggins, Benjamin Harrison Ⓜ Santa Barbara, Calif.; the Hahnemann Medical College and Hospital, Chicago, 1916; specialist certified by the American Board of Internal Medicine; veteran of World War I; for many years on the consulting staff of the Illinois Masonic Hospital and on the attending medical staff, Cook County Hospital in Chicago; served on the staff of St. Francis Hospital in Evanston, Ill.; associated with St. Francis Hospital and the Santa Barbara Cottage Hospital, where he died Dec. 20, aged 70.

Hughes, Archibald William, Greenville, R. I.; Tufts College Medical School, Boston, 1906; died Dec. 10, aged 76.

Hulick, Charles Henry Ⓜ Shelbyville, Ill.; Eclectic Medical College, Cincinnati, 1911; associated with the Shelby County Memorial Hospital; served as president of the Chamber of Commerce; died Dec. 10, aged 70.

Huntley, Howard B. Ⓜ Kindred, N. D.; Northwestern University Medical School, Chicago, 1908; veteran of the Spanish-American War; associated with the St. Luke's Hospital and St. John's Hospital in Fargo, where he died Dec. 2, aged 82.

Jacquet, Edward Frederick, Morgan City, La.; Meharry Medical College, Nashville, Tenn., 1932; on the staff of the Lakewood Hospital, where he died Nov. 13, aged 53.

Jewell, Ernest Lemon Ⓜ Logansville, Wis.; Rush Medical College, Chicago, 1924; past-president of the Sauk County Medical Society; associated with the Reedsburg (Wis.) Municipal Hospital and the Richland Hospital in Richland Center; died Nov. 22, aged 62, of coronary thrombosis.

Jones, Jay Glen Ⓜ Chicago; Northwestern University Medical School, Chicago, 1911; member of the American Academy of General Practice; past-president of the North Shore Branch of the Chicago Medical Society; on the staff of the Grant Hospital, where he died Dec. 13, aged 73.

Kelly, Frank Leo Ⓜ Lieut. Commander, U. S. Navy, retired, Aberdeen, S. D.; St. Louis University School of Medicine, 1916; service member of the American Medical Association; entered the U. S. Navy in 1917 and retired Jan. 1, 1937; member of the American Society of Clinical Pathologists; died in St. Luke's Hospital Sept. 26, aged 67.

Kennedy, Charles Allen Ⓜ Taylorsville, Miss.; Memphis (Tenn.) Hospital Medical College, 1911; member of the American Academy of General Practice; died Dec. 16, aged 72.

Knowles, Donald Brewster Ⓜ Chicago; Northwestern University Medical School, Chicago, 1931; veteran of World War II; member of the Industrial Medical Association; past-president and vice-president of the Chicago Society of Industrial Medicine and Surgery; president of the medical staff of Roseland Community Hospital; on the staff of Jackson Park Hospital; head of the medical staff of the Acme Steel Company in Riverdale; died Dec. 29, aged 51.

Little, Robert Nathan Ⓜ Summerville, Ga.; University of Georgia Medical Department, Augusta, 1929; served as president of the Chattooga County Medical Society; died Dec. 1, aged 55.

Loewenstein, Gustav Joseph Ⓜ Rochester, N. Y.; Albertus-Universität Medizinische Fakultät, Königsberg, Prussia, Germany, 1923; served in the German Army during World War I; associated with Genesee and Park Avenue hospitals; died Dec. 9, aged 61.

Loveland, Horace Hall Ⓜ Escanaba, Mich.; Detroit College of Medicine, 1894; served as health officer of Tecumseh; died Dec. 15, aged 92.

Macdonald, James Herbert, Kennebunk, Maine; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1917; served in World War I as a captain in the medical corps with the Canadian Expeditionary Forces; awarded the Veteran of Foreign Wars "good citizenship medal"; York County medical examiner; a director of the Ocean National Bank and the Kennebunk Building and Loan Association; died in the Maine Medical Center, Portland, Dec. 2, aged 66.

MacKethan, David Gillespie, Fayetteville, N. C.; University College of Medicine, Richmond, 1899; also a druggist; died Dec. 7, aged 80.

McConnell, Thomas William Ⓜ Pittsburgh; Jefferson Medical College of Philadelphia, 1920; served on the staff of the Passavant Hospital; died in St. Clair Memorial Hospital Nov. 18, aged 64.

McIlhatten, Samuel Patterson, Doylestown, Pa.; Medico-Chirurgical College of Philadelphia, 1901; an associate member of the American Medical Association; served on the consulting staff of the Abington (Pa.) Memorial Hospital Dec. 7, aged 79.

McIlwain, Sam Terrell, Waynesboro, Miss.; Mississippi Medical College, Meridian, 1910; served for many years as surgeon for the Gulf, Mobile and Ohio Railroad; died Dec. 26, aged 74.

McNeer, Lewis C. Ⓜ Bristol, Tenn.; Maryland Medical College, Baltimore, 1904; College of Physicians and Surgeons, Baltimore, 1906; on the staff of the Bristol Memorial Hospital; died Dec. 10, aged 80.

Mahan, James Merton Clay Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1913; died Dec. 5, aged 68.

Mansbacher, Kurt Ⓜ St. Louis; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1919; member of the Endocrine Society; served on the faculty of Washington University School of Medicine; a member of the staff of the Jewish Hospital; died Dec. 19, aged 63.

Marshall, Robert Bruce Ⓜ Sulphur, La.; Tulane University of Louisiana School of Medicine, New Orleans, 1927; member of the American Academy of General Practice; on the staff of the West Calcasieu-Cameron Hospital; an honorary member of the board of directors of St. Patrick's Hospital in Lake Charles; died Dec. 9, aged 57.

Martin, Sylvia Parsons Blake, Hackensack, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1897; died in the Holy Name Hospital, Teaneck Nov. 18, aged 85.

Mazique, Zealy Marion, Pine Bluff, Ark.; Meharry Medical College, Nashville, Tenn., 1904; died in the Davis Hospital Dec. 3, aged 83.

Megahan, Calvin Roy, Follansbee, W. Va.; Western Pennsylvania Medical College, Pittsburgh, 1907; member of the West Virginia State Medical Association; past-president and secretary of the Brooke County Medical Society; county health officer and coroner since 1942; died in the Ohio Valley Hospital, Steubenville, Ohio, Dec. 6, aged 74.

Menlowe, Patterson Morris Ⓜ McKeesport, Pa.; University of Pittsburgh School of Medicine, 1923; specialist certified by the American Board of Pathology; member of the College of American Pathologists and the American Society of Clinical Pathologists; associated with the McKeesport Hospital, where he served as medical director and director of laboratory, and where he died Dec. 18, aged 59.

Messmer, Clemens C. Ⓜ Milwaukee; Milwaukee Medical College, 1903; formerly on the faculty of the Marquette University School of Medicine; served on the staffs of St. Joseph's Hospital and St. Michael's Hospital, where he died Dec. 3, aged 77.

Miller, David Isaac, Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; an associate member of the American Medical Association; recently was named "Physician of the Year" by the Dauphin County Medical Society; formerly member of the State House of Representatives; served as medical director of Dauphin County for two terms; associated with the Harrisburg Polyclinic Hospital, where he died Dec. 14, aged 80.

Mitchell, Earl Hix Ⓜ Indianapolis, Ind.; University of Louisville (Ky.) School of Medicine, 1921; member of the American Academy of General Practice; on the staffs of the Community Hospital and the Methodist Hospital, where he died Dec. 20, aged 69.

Morris, Harold Thoes Ⓜ Topeka, Kan.; Northwestern University Medical School, Chicago, 1920; associated with Stormont-Vail Hospital and St. Francis Hospital; died Dec. 3, aged 63.

Morse, Arthur W. Ⓜ Colonel, U. S. Army, retired, Odell, Ill.; Northwestern University Medical School, Chicago, 1899; service member of the American Medical Association; veteran of the Spanish-American War and World War I; entered the regular Army in 1901 and retired Oct. 19, 1920, for disability in line of duty; died in St. James Hospital, Pontiac, Dec. 1, aged 85.

Muir, Walter Francis Ⓜ Browns Valley, Minn.; University of Minnesota Medical School, Minneapolis, 1937; veteran of World War II; associated with the Holy Trinity Hospital in Graceville and the Community Hospital; died in the University Hospitals in Minneapolis Dec. 12, aged 50.

Murray, Charles Kepharte Ⓜ Pittsburgh; University of Pittsburgh School of Medicine, 1919; fellow of the American College of Surgeons; for many years associated with the Columbia Hospital, where he died Dec. 3, aged 66.

Noble, Thomas Benjamin Ⓜ Indianapolis; Washington University School of Medicine, St. Louis, 1918; fellow of the International College of Surgeons; veteran of World War I; associated with the Community, Indianapolis General, and St. Francis hospitals; died in Laguna Beach, Calif., Dec. 8, aged 63.

Osborne, John Carlton Ⓜ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1942; veteran of World War II; instructor in medicine at his alma mater; on the staff of the Mercy Hospital, where he died Dec. 10, aged 42.

Riseborough, Ernest Cecil Ⓜ Detroit; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1918; associated with Warren Diagnostic Hospital; past-president of the Kiwanis Club; served as a director of the Goodwill Industries; died Dec. 3, aged 63.

Ruch, Walter Allwein Ⓜ Memphis, Tenn.; Washington University School of Medicine, St. Louis, 1928; served on the faculty of the University of Tennessee College of Medicine; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served as president of the Memphis Obstetrics and Gynecology Society; on the staffs of the Methodist Hospital, St. Joseph's Hospital, John Gaston Hospital, and the Baptist Memorial Hospital, where he died Dec. 6, aged 63.

Ryan, William Patrick Ⓜ Holyoke, Mass.; University of Vermont College of Medicine, Burlington, 1911; fellow of the American College of Surgeons; veteran of World War I; held the Legion of Honor, Silver Star with Palms, and the French Croix de Guerre; director of health; associated with the Providence Hospital and the Holyoke Hospital, where he died Dec. 2, aged 72.

Smith, Jacob, New York City; Cornell University Medical College, New York City, 1920; associated with the Morrisania Hospital; died Dec. 5, aged 64.

Smith, Stuart Gross Ⓜ Major General, U. S. Army; born in Springfield, Ill., Jan. 11, 1900; Washington University School of Medicine, St. Louis, 1924; two years later accepted a commission in the medical corps reserve; graduate of the Army Medical School and the Medical Field Service School in 1927; Armed Forces Industrial College in 1939; during World War II commanded Vaughn General Hospital, Hines, Ill., before going to Europe where he served with the Civil Affairs Division of SHAEF; later commanded the 97th General Hospital in Germany; from 1946 to 1949 was commanding officer of the Armed Services Medical Procurement Agency, Brooklyn, and was assistant chief and later chief of the supply division in the office of the Army Surgeon General, Washington, D. C., from 1949 to 1951; served as surgeon of the First Army at Governors Island, N. Y., from 1951 to 1953, when he became a surgeon of the Eighth Army in Korea; returned to the United States in June, 1954, to become commanding general, Brooke Army Hospital, Fort Sam Houston, Texas, a position he held until August, 1958, when he became commanding general of Letterman Army Hospital in San Francisco; held the Distinguished Service Medal and the Commendation Ribbon with metal pendant; service member of the American Medical Association; died in the Fitzsimons Army Hospital, Denver, Nov. 19, aged 58.

Soifer, Samuel Ⓜ Forest Hills, N. Y.; born Nov. 24, 1899; University and Bellevue Hospital Medical College, New York City, 1924; specialist certified by the American Board of Urology; fellow of the International College of Surgeons; veteran of World Wars I and II; member of the Association of Military Surgeons of the United States; on the faculty of the State University of New York College of Medicine at New York City; associated with the Goldwater Memorial Hospital in New York City, Kings County Hospital in Brooklyn, and Terrace Heights Hospital in Hollis; died Dec. 4, aged 59.

Spiegel, Samuel Ⓜ New York City; Bellevue Hospital Medical College, New York City, 1898; fellow of the American College of Surgeons; on the staff of the People's Hospital; died Dec. 6, aged 81.

Steingrube, C. Roy, Cincinnati; University of Cincinnati College of Medicine, 1929; member of the Ohio State Medical Association; county health commissioner; formerly member of the county board of health; associated with the Deaconess Hospital; died Dec. 2, aged 55.

Stewart, Clinton George Ⓜ Circleville, Ohio; Rush Medical College, Chicago, 1912; served on the Pickaway County Library Board; associated with the Berger Hospital; died Nov. 1, aged 85.

Stouffer, John Franklin Ⓜ Philadelphia; Medico-Chirurgical College of Philadelphia, 1915; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; for many years associated with the Philadelphia General Hospital; died in the Bristol (Va.) Memorial Hospital Nov. 2, aged 76.

Streysman, Francis Edward Ⓜ Oaklawn, Ill.; Loyola University School of Medicine, Chicago, 1931; police surgeon for the village of Hickory Hills; on the staff of the Holy Cross Hospital in Chicago; died Nov. 15, aged 64.

Summerville, William Eugene Ⓜ Louisville, Ky.; University of Louisville School of Medicine, 1925; member of the Southeastern Surgical Congress; served as surgeon for the Louisville and Nashville, Kentucky and Indiana Terminal, and Illinois Central railroads; on the staff of SS. Mary and Elizabeth Hospital and past chief of staff there; associated with St. Joseph Infirmary; died Nov. 11, aged 58.

Swickard, George Yeagley Ⓜ Orange, Texas; Ohio State University College of Medicine, Columbus, 1931; associated with the E. I. du Pont de Nemours and Company; member of the Industrial Medical Association; chief of the surgical staff at the Orange Memorial Hospital where he died Nov. 22, aged 52.

Thomas, Carlyle Milton Ⓜ Bangor, Pa.; Jefferson Medical College of Philadelphia, 1926; school physician in Bangor; for many years school physician; associated with St. Luke's Hospital in Bethlehem and Easton (Pa.) Hospital; died Dec. 6, aged 57.

Torrey, Eugene Weiss Ⓜ Baltimore; Jefferson Medical College of Philadelphia, 1917; service member of the American Medical Association; veteran of World War I; for many years associated with the Veterans Administration; member of the Endocrine Society and the American Psychiatric Association; died in the Veterans Administration Hospital Nov. 12, aged 65.

Van Sweringen, Walter Ⓜ Amarillo, Texas; University of Maryland School of Medicine, Baltimore, 1904; member of the Radiological Society of North America; served in France during World War I; at times on the staffs of Northwest Texas Hospital and St. Anthony's Hospital; died Nov. 16, aged 78.

Waldman, Irwin Jerome Ⓜ Milwaukee; University of Illinois College of Medicine, Chicago, 1934; service member of the American Medical Association; specialist certified by the American Board of Obstetrics and Gynecology; physician at the regional office of the Veterans Administration; died in the Milwaukee Sanitarium Foundation, Wauwatosa, Nov. 8, aged 49.

Weller, Theodore Warford Ⓜ Oakland, Calif.; Harvard Medical School, Boston, 1924; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; veteran of World War I; associated with the Samuel Merritt Hospital, Peralta Hospital, and the Providence Hospital, where he was president of the medical staff, and where he died Dec. 10, aged 64.

Wezeman, Paul Henry Ⓜ Oak Park, Ill.; Chicago College of Medicine and Surgery, 1914; for many years on the staff of the West Suburban Hospital, where he died Dec. 21, aged 75.

Whitefort, Arthur Rand Ⓜ St. Elmo, Ill.; St. Louis University School of Medicine, 1905; member of the American Academy of General Practice; served as president of the Fayette County Bank; associated with St. Anthony's Hospital in Effingham, and Fayette County Hospital in Vandalia, where he died Nov. 8, aged 78.

Williams, Christopher Smith, La Fayette, N. Y.; University of Buffalo School of Medicine, 1897; an associate member of the American Medical Association; past-president of the Syracuse Academy of Medicine and the Onondaga County Medical Society; health officer of the town of LaFayette; served on the staff of the Crouse-Irving Hospital in Syracuse; died Dec. 6, aged 86.

Wilson, Gustave Ⓜ Sacramento, Calif.; born in Stockholm, Sweden, Aug. 13, 1875; University of Michigan Homeopathic Medical School, Ann Arbor, 1903; fellow of the American College of Surgeons; past-president of the Sacramento Society for Medical Improvement; member of the California Medical Advisory Board during World War I; formerly member of the state board of health; served on the county health and welfare board, which he helped to establish; for many years a director of the Sacramento Merchants National Bank; formerly assistant superintendent of the Patton (Calif.) State Hospital; member and for many years vice-president of the board of trustees of the Sutter Hospital, where he was a member of the staff, and where he died Dec. 3, aged 83.

Wood, Harold Bacon Ⓜ Harrisburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; fellow of the American Public Health Association; at one time epidemiologist for the New York State Department of Health and the Pennsylvania Department of Health; formerly health officer of Bloomington, Ill.; served on the faculty of his alma mater; author of "Sanitation Practically Applied"; died Dec. 1, aged 80.

York, William Edward Ⓜ Giddings, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1894; died Dec. 7, aged 88.

Zeigler, Jerome Ⓜ Cincinnati; University of Cincinnati College of Medicine, 1920; member of the American Academy of General Practice; clinical instructor in medicine at the University of Cincinnati College of Medicine; member of the staff of the Bethesda Hospital, where he died Dec. 6, aged 63.

FOREIGN LETTERS

BRAZIL

Blood Groups Among Brazilian Indians.—Several studies were made of blood groups among Brazilian Indians. In the State of Paraná, Dr. L. Fernandes found that of 77 Caingangues Indians 81.6% belonged to blood group O, 13.1% to group B, and 5.3% to group A. Among 119 Bororós and 237 Caiuiás Indians in the state of Mato Grosso, Dr. L. Ribeiro and co-workers observed the same predominance of group O. More recently a study of 71 Indians living at Porto Capitão Vasconcelos in the state of Amazonas by Dr. G. M. Leite and co-workers of the University of São Paulo (*Revista paulista de medicina*, vol. 53, November, 1958) showed that all belonged to group O. The MN factors were distributed as follows: M, 46%; N, 4%; and MN, 50%. All were Rh positive.

Fungi in Gallbladder.—At the Institute of Mycology in Recife, Dr. A. C. Batista and co-workers (*Revista da Associacão médica brasileira*, vol. 4, October, 1958) found Candida and Cryptococcus in the bile of 21 of 33 patients with cholecystitis. They examined 109 samples of bile. Differences between microscopic results and the ones with culture mediums were ascribed to the use of tetracycline in the mediums to prevent bacterial growth. These findings may have a bearing on the etiology of cholelithiasis and on some allergic manifestations of unknown origin.

Asthma Treated with Hypnosis.—Dr. A. C. M. Passos, of the Escola Paulista de Medicina of São Paulo (*Revista brasileira de tuberculose*, vol. 26, December, 1958), induced hypnosis in three patients with asthma. One was treated by prolonged suggested sleep (19 hours a day) for 60 days, with excellent result. The others were treated by direct suggestion of relaxation for 30 to 60 min. They also obtained favorable results.

GERMANY

Diagnostic Errors in Bronchial Carcinoma.—In some patients it is difficult to diagnose bronchial carcinoma correctly, especially early in the course of the disease. For this reason an exploratory thoracotomy is often necessary. Becker and Knothe (*Thoraxchirurgie* 6:235, 1958) investigated a series of 443 patients who were subjected to thoracotomy and whose conditions had been diagnosed as bronchial carcinoma at the surgical clinic of Giessen University. There were 18 diagnostic errors among 256 resections (7.1%) and 4 among 190 thoracotomies (2.1%). Ten patients had chronic pneumonitis, six tuberculosis, three a benign bronchial tumor, one Hodgkin's disease, and in two the diagnosis could not be determined. As most of these conditions required surgical treatment little harm was done by performing the thoracotomy, but in some of the patients a correct diagnosis would have prevented resection of a whole lobe. In six patients the wrong diagnosis was due to preoperative and/or intraoperative histological examination. In many cases the cause of histological diagnostic errors was that too little material was obtained for examination. Because of these diagnostic errors, sputum examination and/or bronchoscopy are no longer relied on and a pulmonary biopsy specimen should be obtained for final verification of the diagnosis.

Isoniazid Resistance.—Along with the decrease in mortality from pulmonary tuberculosis, an increase in the number of incurable cases of open tuberculosis has been noted. To reduce the risk that such patients constitute as potential sources of infection, it is necessary to expand control programs insofar as possible. The possibility of reducing the virulence of the Mycobacterium tuberculosis discharged by these people is being explored. The virulence of highly isoniazid-resistant tubercle bacilli is usually greatly diminished. H. Bierschenk (*Ztschr. Tuberk.* 111:159, 1958) reporting on a study of 37 patients with open tuberculosis, 13 of whom had tubercle bacilli of normal sensitivity in their sputums, concluded that isoniazid-resistant tubercle bacilli rarely cause disease unless the infecting dose is extremely high or the patient is particularly susceptible. Continuous administration of isoniazid reduces the danger of the nonisolated patient with open incurable tuberculosis as a source of infection. The time required and degree of the decrease of infectivity cannot be predicted but the time is probably several months.

Cancer in Childhood.—Among the causes of death in childhood, infectious diseases have ceased to predominate. Fatal accidents now hold first place. They are followed in order of frequency, in all civilized countries, by malignant disease, including leukemia, lymphosarcomatoses, carcinoma, and sarcoma. In the state of North Rhine–Westphalia, the number of deaths from malignant disease has

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The items in these letters are contributed by regular correspondents in the various foreign countries.

superseded that from tuberculosis. In children aged 6 to 15 malignant disease ranks higher than pneumonia and tuberculosis combined. In the whole Federal Republic, this marked increase in mortality from tumors and leukemia has been observed among infants and children since 1951. It is only partly relative, i. e., explained by the decreasing mortality from infectious diseases. E. F. Hugh (*Ärztl. Wschr.* 13:990, 1958) surveyed the tumor localizations of patients at the children's clinic of the medical academy at Düsseldorf and found in the order of descending frequency: leukemia and tumors of the brain, kidney, soft tissues, eye, and bones. Some of the most frequent tumors of children were distinguished from those of adults by being genuinely embryonal. Preventive measures recommended include the exclusion of all carcinogenic agents from both mother and child, and avoidance of exposure of infants to x-rays. It is not sensible to protect the fetus in utero from x-rays only to expose the infant after birth to unnecessary radiologic examinations.

INDIA

Lung Surgery.—P. Singh (*Indian Journal of Surgery*, vol. 20, October, 1958) analyzed a series of 238 patients subjected to lung surgery. In most of them the pulse rate was well stabilized preoperatively. A few because of a high pulse rate had to be operated on in two stages at an interval of two to three days and did well even when the preoperative pulse rate was 100 to 140. Some had a high temperature at the time of operation and these were also operated on in two stages. Breath-holding time was another preoperative criterion, a patient with a breath-holding time of 45 seconds or more being considered an excellent risk; one with 30 to 45 seconds, a good risk; and one with less than 30 seconds, a poor risk. Patients with a breath-holding time of over 30 seconds and vital capacity of over 2 liters usually behaved well during the operation. An exercise tolerance test was made on 37 patients and served as a useful guide to physical status. A hemoglobin level of 10 to 15 Gm. was considered favorable, although occasionally patients with lower values had to be operated on. Most of the patients before operation had a sedimentation rate of less than 20 mm.

In most patients anesthesia was induced with thiopental and maintained with nitrous oxide, oxygen, and ether. Tracheal obstruction by secretions was not common as most of the patients were well prepared by regular postural drainage but some required bronchoscopic aspiration before anesthesia. Postoperative complications, besides shock and hemorrhage, included subcutaneous emphysema, mediastinal emphysema, pneumothorax, contralateral spontaneous pneumothorax, mediastinal displacement, paradoxical respiration, tachycardia, arrhythmias, retained secretions, pulmonary edema, atelectasis, laryngotracheal bronchitis, pulmonary infections, hydrothorax, and acute dilatation of the stomach. There were 10 deaths in the series, 7 due to shock, 1 due to anuria, and 2 unexplained.

Sulfamethoxypyridazine.—P. G. Kamath and coworkers (*Indian Journal of Medical Sciences*, vol. 12, November, 1958) treated 28 patients who had acute urinary and respiratory tract infections with sulfamethoxypyridazine, a long-acting sulfonamide. Only those who were not previously treated by other sulfonamides or antibiotics were included. The drug was given orally, the common dosage schedule being 1 Gm. as initial dose, followed by 0.5 Gm. daily. In severe cases 2 Gm. was given initially, followed by 1 Gm. daily. The larger dosage was also used when there was no response to the lower dosage within two or three days. The duration of treatment varied from 4 to 16 days. A good response was observed in 21, a poor or no response in 3, and in 4 the drug had to be discontinued because of toxic effects. The series included 15 patients with lobar pneumonia, 12 of whom showed a good response. The fever subsided on an average within 32 hours and the cough and pain in the chest subsided within three or four days. Of the three who failed to respond, two developed acute mania, one on the second day and one on the third day, and one developed hemorrhage and oliguria. There were six patients with bronchitis, all of whom showed a good response. One patient in this group complained of mild headache.

Of the four patients who had urinary tract infection with Escherichia coli or Proteus vulgaris, only one patient suffering from pyelitis due to P. vulgaris responded to the drug, the fever subsiding in six days and the pyuria showing a decrease. The urine cleared completely after 14 days, at which time urine culture was negative. The other three showed no improvement even after administration of the drug for 12 days. Of the remaining three patients one had a congenital cystic lung, one bronchiectasis, and one bacillary dysentery. The last two responded well but the first, after an initial improvement, developed acute delirium on the third day and this form of treatment was stopped. The clinical results of this drug in infections of respiratory tract were comparable to those with sulfadiazine. The number of pneumonia patients developing psychosis during treatment was, however, alarming.

Parekh and Adiga in the same journal reported the use of this drug in a series of 84 patients and 40 normal controls. Eight of the patients developed psychotic manifestations but the severity of infection could not be held responsible for these symptoms. Two had received only small doses of the drug and the duration of therapy was short.

Ony one patient gave a family history of mental illness. The toxic effects were attributed to the presence of a pyridine and a methyl group in the drug and the occurrence of psychosis in none of the controls suggested the possibility of the anoxia occurring in pneumonia having some relation to the toxicity of the drug.

Bone and Joint Lesions in Smallpox.—The *Indian Journal of Surgery* (vol. 20, October, 1958) contained a study of 10 subacute cases of smallpox arthritis uncomplicated by sinus formation. Biopsies of bone, muscle, joint capsule, and synovial membrane were performed to determine the kind of lesions present. Fluid aspirated from the joints was cultured. Clinically these cases resembled those of pyogenic arthritis except for absence of fever. Bilateral involvement and affection of elbow joints were common findings. Cases coming one to two years after the attack of smallpox showed fibrous ankylosis, and those coming seven or eight years later showed disturbances of growth, although there was a surprising amount of movement in the affected parts. Bony ankylosis occurred only if there was secondary infection after sinus formation.

The radiologic features in the subacute stage resembled those of chronic pyogenic arthritis except that both contiguous ends of the bones forming the joint were involved. Cystic changes and subperiosteal bone formation without sequestrums and without marked necrosis and new bone formation were characteristic features. Both epiphysis and metaphysis were involved along with the joint, and isolated bone involvement was rare. Joint changes consisted of increase in joint space and erosion of articular ends with some periarticular soft tissue swelling. In late cases the joint space was diminished with deformed articular ends, and, in some, scalloped ends with widening of the joint space was noticed.

Cultures of aspirated material and of tissues removed at biopsy were sterile. The microscopic appearance of the bone resembled that of osteitis fibrosa with occasional round cell infiltration. Soft tissues such as muscle, synovial membrane, and fascia showed fibrosis, hemorrhage, and round cell infiltration. The purely osseous lesions improved with scraping and curettage. Partial excision was performed in the osteoarticular type when satisfactory movement was obtained in the elbow in one patient and in another this operation was a failure. Nonspecific protein therapy and active use in a late case caused improvement in the range of movement. Eight early cases with swollen and tense joints improved with splinting and rest. One patient with bony ankylosis was subjected to manipulation under anesthesia to improve the angle of ankylosis. During follow-up study of these cases, a gradual improvement in the range of movements without any recurrence of inflammation was noticed. Deformities due to epiphysial damage tended to increase during the growth period requiring osteotomy in one patient for correction of valgus deformity at the knee joint.

Auxiliary Nursing.—A brighter future for the auxiliary nurse and better training for this type of health worker were called for at the 12-nation conference of auxiliary nursing sponsored by World Health Organization in December in New Delhi. It was suggested that local nursing school committees be set up to meet the needs of health services by improving local recruitment. The main purpose of such committees would be to inform the public about nursing training and services and to make living and service conditions of nursing workers attractive. At ministry level a nursing board or council would be able to encourage recruitment in the state or country as a whole. One group suggested that the registration of auxiliary nurses was desirable. Every auxiliary nurse should receive basic training to prepare her to act as an assistant nurse. Such assistant nurses could be employed in institutions where day-to-day supervision by trained nurses was available. For workers to be assigned to such specialized fields as tuberculosis, a further period of training would be necessary.

Health Aspects of Radiation.—A new step towards establishing India as a training center for southeastern Asian workers in the health aspects of radiation and atomic energy was taken in November when about 20 students from three southeastern Asian countries began a five-week course in health physics in Bombay. There were also four participants from the western Pacific region. This course is designed for physicists who will serve as supervisors and instructors in radiation protection. It is sponsored by the Indian Department of Atomic Energy and the World Health Organization with the cooperation of the Atomic Energy Commission of the United States.

Fractures of the Neck of the Femur.—Bhansali and Dholakia treated 30 patients with fracture of the true neck of the femur, their ages varying from just below 20 to 80 years. Three had valgus and 27 had varus fractures. The injury responsible for most of the fractures was an accidental fall while walking, running, or alighting from a train. The method of treatment depended on the type of fracture as seen radiologically, the duration of the fracture, the presence or absence of complications, the age of the patient, and the economic circumstances. The three patients with the valgus fractures were treated with simple bed rest, the limb being kept in a neutral position with the help of sandbags for three months. Smith-Peterson nailing was performed in 16 patients, in 5 of whom secondary operations were required. The shortest time between injury and operation was 2 and the longest 30 days. A plaster boot with a wooden board incorporated in its posterior part was applied immediately after the nailing to keep the limb in a position of internal rotation. Antibiotics were given routinely to all patients. Static quadriceps exercises were started on the same day or the next. On the third day the knee on the affected side was moved after turning the patient on the sound side. The patient was made to sit up in bed on the 4th or 5th day and the plaster boot was removed on the 12th to 14th day. Weight-bearing on the affected side was not allowed till there was radiologic evidence of sound bony union. There were three deaths in this series.

Fibrocongestive Splenomegaly.—Goyal and Gupta (*Current Medical Practice*, vol. 2, November, 1958) stated that the cause of Banti's disease is still controversial. Such factors as portal hypertension, chronic intoxication, and allergy have been considered. The authors studied the role of allergy in patients and experimental animals. Of 100 specimens from spleens removed at operation or autopsy, 37 showed the lesions of malaria, 30 formed a miscellaneous group, in 15 the enlargement was due to congestive heart failure, 13 showed varying degrees of fibrosis and congestion, and 5 showed the lesions of tropical splenomegaly. Spleens weighing 150 Gm. or more and showing evidence of fibrosis and congestion were classified as cases of Banti's disease. The liver and portal veins could be examined in 13 cases and only 6 of these showed evidence of portal obstruction; 2 were due to right-sided failure and 5 were from patients with such infections as bronchiectasis and tuberculosis. Thus all the cases of Banti's disease were not due to portal obstruction.

To determine the role of allergy in causing fibrocongestive splenomegaly, repeated injections of sheep serum were given to rabbits and repeated injections of tuberculin were given to a series of guinea pigs rendered allergic by previous injection of BCG vaccine. No splenomegaly developed in the rabbits although all spleens in rabbits that were killed from the 10th week onward showed fairly marked congestion and fibrosis. The spleen in guinea pigs also showed no enlargement, but there was microscopic evidence of congestion and a certain degree of reticuloendothelial hyperplasia with presence of hemosiderin in macrophages and extracellularly. Fibrosis was evident seven weeks after the commencement of the tuberculin injections. Thus allergy probably played some part although absence of marked enlargement indicated that it alone could not be responsible when there was no portal obstruction.

Surgical Ascariasis.—A. E. deSa (*Indian Journal of Child Health*, vol. 7, November, 1958) reported a series of 43 cases of roundworm obstruction in children. Surgical ascariasis was found to be the second largest cause of intestinal obstruction in children, the first being imperforate anus. The age of these patients varied between 2 and 10 years. Abdominal pain, vomiting, constipation, and fever were the most frequent symptoms, others being distention, drowsiness, and roundworms in vomitus and stools. The three most frequent signs of ascarideal obstruction in this series were the presence of a palpable and occasionally a visible mass, fever, and toxemia. The roundworm mass tended to be central, migrating from one part of the abdomen to another and frequently breaking up into two or more masses. The toxemia closely resembled that of typhoid with apathy, delirium, and muscular twitching. This was often dramatically relieved by intravenous administration of 25 cc. of 50% dextrose solution. The fever rarely exceeded 101 F (38.33 C). Increase in the eosinophilic count was not a reliable diagnostic sign.

Of the four types of obstruction attributed to ascaris (mechanical, spastic, ascarideal intussusception, and ascarideal volvulus), only the first two were observed in this series. There was only one case of spastic obstruction among the patients operated on, the walls of the ileum being powerfully contracted on a roundworm lying longitudinally inside so as to produce marked obstruction. The obstruction was commonly due to a firmly packed bolus of worms with the antimesenteric border showing areas of ischemia and gangrene when the lump was big. Proximal distention was never as pronounced as in other organic intestinal obstructions.

In one child a large number of the roundworms had found their way into the general peritoneal cavity through a pinpoint opening in the tip of the appendix, while in another no perforation was found in any part of the gastrointestinal tract, but the general peritoneal cavity was full of worms. Neither patient showed any peritoneal reaction, the edges of the perforation in the former being smooth, bleeding readily, and free of any fibrinous deposits. A chronic intraperitoneal abscess was occasionally seen after an indolent roundworm perforation. Thus one patient was brought in because of a liver abscess, the live roundworm wriggling out of the drainage opening after incision.

The author favored conservative treatment of these patients with operation only when the diagnosis is in doubt, perforation is diagnosed or suspected, distention is pronounced and progressive, or when conservative management has failed to relieve the distention and the general condition deteriorates. Conservative management includes correction of fluid and electrolyte imbalance by parenteral fluid administration, continuous gastric suction, daily saline enema, administration of atropine to counteract spasm, intravenous infusion of 25% dextrose solution for the toxemia and the administration of specific anthelmintics and suitable antibiotics. Of the 34 patients who were treated conservatively 28 were given santonin and calomel at night, followed by a simple enema next morning and a small dose of magnesium sulphate if it was found to be safe. This treatment was repeated once in one case and twice in another; six patients were given hetrazan syrup. The roundworms were generally passed within 24 hours and no purgation was required. The fact that purgation was not necessary with hetrazan as with santonin was a distinct advantage. In two patients the roundworms were passed soon after an intramuscular injection of 0.3 or 0.4 mg. of atropine. Penicillin and streptomycin were given routinely to combat associated infection. Six patients were operated on, three of whom died. Of the 34 treated conservatively, six died. In a patient with Meckel's diverticulum with a band obstruction roundworms crawled out of the umbilicus. This patient was operated on and died. The author stressed the inadvisability of early operation as most patients respond to conservative treatment.

Family Planning Program.—The Family Board requested that a tentative provision of $2,100,000 be made by the Government of India for the implementation of the Family Planning Program during the fiscal year 1959-1960. The main feature of this program would be an intensification of training and educational schemes, opening and maintenance of clinics, appointment of family planning education leaders, holding of orientation camps, free distribution of contraceptives through all primary health centers and medical institutions, strengthening of the institutions, and strengthening of the inspection organization and research. The number of clinics so far opened is 718. Against the target of 150 urban and 600 rural clinics by March, 1959, 171 urban and 400 rural clinics have been started. The state governments hope to open 151 additional rural clinics before March.

Leprosy.—Kelkar and Randive (*Indian Journal of Medical Sciences*, vol. 12, November, 1958) stated that many unsuccessful attempts have been made to transmit human leprosy to laboratory animals. They studied the role of such factors as age, repeated contact, and general resistance. Because children are known to be more susceptible to the disease than adults, newborn animals (75 rats, 36 hamsters, and 24 mice) were given multiple inoculations of human lepromatous material. The general resistance is on an average low in the tropics and subtropics where this disease is common. The body resistance of the laboratory animals was lowered by giving cortisone, feeding a diet deficient in vitamin B_1, sensitization with lepromin, administration of hyaluronidase, and exposure to x-rays. The inoculum consisted of a human lepromatous nodule and a suspension of human lepra bacilli. The nodule was inoculated subcutaneously and the suspension intramuscularly or intraperitoneally. Young adult rats thus inoculated served as controls. Both the groups were observed for 8 to 18 months.

The hamsters, 7 of which served as controls, were treated with varying doses of x-ray. Both the groups were observed for six months and killed when the animals looked emaciated. Of the 75 rats, 42 showed acid-fast granules in their tissue cells and a nonspecific cellular reaction which was mainly of a defensive inflammatory nature. The few organisms seen were in and around nerves, and a large number of acid-fast granules were seen in macrophages with diffuse pink cytoplasm. The control rats and those treated with cortisone and a vitamin B_1-deficient diet did not show any significant difference in their tissue reaction to repeated inoculation of human lepromatous material. The reaction, however, was more pronounced and a larger number of animals was affected when cortisone and a vitamin B_1-deficiency diet was given prior to inoculation.

The intraperitoneal inoculation of human lepra bacilli was found to be more effective than inoculation by any other route. There was a complete absence of tissue reaction in the mice treated with hyaluronidase or lepromin prior to inoculation. A study of tissue reactions in the hamsters showed evidence of survival, maintenance, and even proliferation of acid-fast organisms in over 50% of those in the irradiated group. Such evidence was absent in those treated with cortisone and in the controls. In young hamsters showing evidence of disease, the bacilli were liberated into the subcutaneous tissue after disintegration of the transplanted lepromatous nodule. Some bacilli were ingested by macrophages and others transported to regional axillary lymph nodes via lymphatics where they were again engulfed by macrophages and other cells of the reticuloendithelial system. The older hamsters so treated showed marked tissue damage. The tissue reactions suggested a progressive generalized infection. A dose of 100 r whole body irradiation given to young adult hamsters prior to inoculation of lepra bacilli thus proved to be a means of lowering body resistance of these animals to leprosy.

Anemia and Kwashiorkor.—Ismail and Chandra (*Indian Journal of Child Health*, vol. 7, November, 1958) treated 50 patients who had iron-deficiency anemia with intramuscular injections of an iron-dextran complex. These patients were divided into those in whom the iron deficiency was not associated with kwashiorkor (30) and those who had both conditions (20). The total dosage of elemental iron ranged from 700 to 1,200 mg. A 22-gauge needle of sufficient length to penetrate well beyond the superficial tissues and fat layers was used so as to ensure that the pool of iron was placed deeply into the muscle and to prevent it from leaking back into the subcutaneous tissues. The patients showed the usual clinical features of iron-deficiency anemia but koilonychia was rare. Glossitis, pigmentation, and dysphagia were also uncommon. In the first group 25 patients had a history of malnutrition, 13 of ascariasis, 8 of malaria, and 13 of repeated attacks of diarrhea. Three had active tuberculosis, one with tuberculous meningitis; seven had other respiratory infections, two urinary infections, and four hookworm infestation. In the second group 16 had a history of malnutrition, 12 of ascariasis, 8 of malaria, and 17 of repeated attacks of diarrhea. Two had tuberculosis and five had other respiratory infections. No patient was below one year of age.

The initial hemoglobin level in the first group varied from 20 to 50%. The average rise in the first week was 10% while over a four-week period the maximum rise was 60% and the minimum 10%. In the second group the initial hemoglobin level was 20 to 60% and the average rise during the first week was 8%, the maximum response being 30%. The red blood cell counts varied from 1.5 to 3 million in the first group and showed an average rise of 1.5 million in four weeks. The erythrocyte count and the PCV rose more rapidly than the hemoglobin level. In the second group, the initial erythrocyte count varied from 1 to 3.5 million and rose by 1.25 million after four weeks. Macrocytes and target cells were seen in the blood smears in many patients, indicating that the anemia in kwashiorkor may be of a mixed type. The bone marrow in the first group was typical of microcytic anemia with normoblastic reaction and in the second group the findings were those of a macronormoblastic reaction without any megaloblasts. The initial serum iron level showed great variation, the mean value being 50 mcg. per 100 ml.

After treatment, serum iron levels of 64 to 400 mcg. per 100 ml. and above were recorded. The total plasma proteins were low in both groups and the albumin/globulin ratio was altered. These changes were more marked in the second group but they were not related to the clinical features of the kwashiorkor or the severity of the anemia. Toxic reactions and local side-effects were almost absent. No allergic or pyrogenic reactions occurred. The advantages over oral iron therapy were that the absorption was not limited by the activity of the mucosal barrier, there was no likelihood of the treatment being suddenly discontinued, and a known quantity of iron could be given ensuring a rapid response.

Typhoid in Children.—Paul and Jatkar (*Indian Journal of Child Health*, vol. 7, November, 1958) found that of 2,000 admissions to the K. S. Children's Hospital, New Delhi, over a period of 21 months, 56 were for typhoid. Only two of these patients were between 1 and 2 years old. The highest incidence was between 5 and 9. The greatest number of cases were seen in June, July, and August. Two patients had had triple typhoid vaccination 1 and 2 years, respectively, prior to admission. A history of contact was available in six patients. The temperature did not follow any particular pattern, high, moderate, and low remittent grades being commoner than intermittent. Blood cultures positive for Salmonella typhosa were obtained in 37 cases. The Widal test was positive in titers of 1:60 to 1:3,200 in 25 patients. This test was not run on all patients with positive blood cultures and some who had positive blood cultures did not show a rise in titer.

The leukocyte count varied from a marked leukopenia to leukocytosis. A normal count was restored in those with leukopenia after treatment with chloramphenicol. The polymorphonuclear count varied from 40 to 80%. Three patients suffered a relapse which responded to a second course of chloramphenicol. There were four deaths, one due to encephalopathy, one to hepatitis, one to bronchopneumonia, and one to uncontrolled diarrhea. A full diet was given as soon as possible, usually within two or three days of admission, when the toxemia and fever abated. Three consecutive negative stool cultures at weekly intervals were considered necessary before discharging the patient. Typhoid fever is so common in India that it must be considered in all patients whose fever lasts more than three days.

Meprobamate in Tetanus.—Damany and Kamat (*Journal of the Indian Medical Association*, vol. 31, Nov. 16, 1958) stated that a fully conscious mind with the painful awareness of spasms probably increases the frequency of spasms and rigidity in tetanus. Tranquilization has therefore been considered essential in the treatment of this disease. The centrally acting sedatives commonly used have the danger of producing central depression. None of the muscle relaxants acting peripherally have proved uniformly successful and some of them also give rise to dangerous side-effects such as hemoglobinuria and pulmonary edema.

The authors therefore studied the usefulness of meprobamate which has both muscle relaxing and ataractic action, is orally effective, and has low toxicity. In their series of 66 patients with tetanus, 27 received the usual treatment with tetanus antitoxin, antibiotics, and sedation, and 39 received meprobamate in addition. The drug was given orally in six hourly doses of 800 mg. in adults till cure or death occurred. It was omitted temporarily in those who showed complications. Patients with a period of onset of spasms of less than 24 hours showed a higher mortality in both groups (50% in the first group and 33% in the second)' than those with the period of onset longer than 24 hours (19.1% in the first group and 18.5% in the second).

The duration of stay in hospital of those who survived varied from 8 to 26 days in both groups. Death in most of those who died occurred within 48 hours of admission. The percentage survival rate was a little better in the second group than in the first but meprobamate did not alter the course of the disease significantly. Whatever beneficial influence it had was seen only in mild and moderate types of cases, while the severer type was unaffected. Its tranquilizing and muscle relaxing action was apparently not strong enough to control the spasms and rigidity of tetanus. Another disadvantage was the prolonged period before its effects became manifest. No serious side-effects were attributed to the drug.

SWEDEN

Basophils in Asthma, Dermatitis, and Psoriasis.—The average basophil count in the peripheral blood of 20 patients with asthma, 30 with atopic dermatitis, and 22 with nonerythrodermic psoriasis was studied by Hans Rorsman (*Acta dermat.-venereol.* 38:175, 1958) to determine whether the decrease of basophils observed in urticaria was characteristic of allergic diseases or diseases of the skin. The control group consisted of 96 normal persons. None of the patients had an average count which significantly differed from the mean count of 44.8 ± 2.4 per cubic millimeter in the controls, but 5 patients with exfoliative erythroderma had an average of 95.6 basophils per cubic millimeter (range 42 to 214).

Exposure of Ruptured Lumbar Disks.—Carl Hirsch (*Acta orthop. scandinav.* 28:76, 1958) stated that hypotension keeps bleeding under control while disk surgery is in progress and offers a good view of the exposed area. It also protects against postoperative hematoma. This approach should limit the damage to important functional elements. By making the incision in the dorsal fascia lateral to the spinous processes and closing the wound with the spine flexed, postoperative tightness is less pronounced. Extensive disk removal protects against disk material being squeezed out when early weight-bearing is permitted. The patient is allowed out of bed after the operation. No physiotherapy, no support, and no fusion are needed.

Oxygen Saturation of the Cord Blood.—The oxygen saturation in the blood of the umbilical cord was measured with the Brinkman Haemoreflektor in 90 cases of cesarean section, of which 16 were classified as complicated and 74 as uncomplicated by Sjöstedt and Rooth (*Acta anæsth. scandinav.* 2:99, 1958). In uncomplicated cases in patients delivered under local anesthesia before the onset of pains, the oxygen saturation in the vein was 62.1%, and in the arteries 32.4%, i. e., the same values as in uncomplicated spontaneous deliveries. With the onset of pains the oxygen saturation decreased. Inhalation anesthesia with cyclopropane resulted in a marked depression of the oxygen saturation of the fetal blood and diminished the arteriovenous difference in the oxygen saturation, which led the authors to conclude that when local anesthesia can be used without risk to the mother this method is best for the infant.

Adrenocortical Hyperplasia.—A family consisting of normal parents, three healthy children, and three children with congenital hyperplasia of the adrenal cortex was studied clinically and analyses of their steroid excretion were made by G. Birke and coworkers (*Acta endocrinol.* 29:55, 1958). The parents and the three healthy children exhibited a normal excretion pattern of all steroid groups studied. One of the three affected children died at the age of 8 weeks before any steroid analysis could be undertaken. The other two children with adrenocortical hyperplasia showed a substantially increased excretion of both 17-ketosteroids and 17-hydroxycorticosteroids and pathologically altered excretion patterns. Of the individual 17-ketosteroids, androsterone was predominant and little, of any, etiocholanolone could be found. Of the individual 11-oxygenated 17-ketosteroids, 11-ketoandrosterone and 11β-hydroxyandrosterone were isolated and identified by infrared spectroscopy; 11-hydroxyetiocholanolone could not be detected. An indirect analysis of the 17-hydroxycorticosteroid pattern revealed the presence of huge amounts of pregnanetriol. Measurable amounts of tetrahydro-17α-hydroxycortexone tetrahydro-S) were also demonstrated in the urine. In neither of the two children was the excretion of the latter accompanied by hypertension. Tetrahydrocortisone and 11-ketopregnanetriol or cortolone were also identified, but no 11β-hydroxylated corticosteroids could be detected. The preoperative estrogen pattern was characterized in both patients by the complete absence of estriol. After bilateral adrenalectomy substantial amounts of estriol were detected in the urine in the case of a female pseudohermaphrodite, aged 15, with adrenocortical hyperplasia treated first by excision of the clitoris, then by bilateral subtotal adrenalectomy when cortisone in the dosage required for suppressing the adrenocortical secretion gave rise to mental symptoms.

Treatment of Salicylate Intoxications.—Celander and Haglund (*Acta anæsth. scandinav.* 2:123, 1958) used a combination of neuromuscular block, artificial respiration, and fluid and electrolyte therapy to treat severe salicylate intoxication. Of 20 patients treated 15 were under 6 years of age. A liberal supply of fluid and calories in the form of an intravenous dextrose solution was given while further clinical and laboratory analyses were being made. Controlled respiration combined with neuromuscular block when respiratory failure threatened was essential. Tubocurarine was used as the neuromuscular blocking agent. Tracheotomy was performed and artificial respiration maintained with the Gothia respirator. In no case was respirator treatment necessary for more than two days. During that time, the patient was allowed the necessary muscular rest, the acid-base disturbances were corrected, and salicylate excretion was achieved.

Myocardial Infarction.—Gunnar Biörck and co-workers (*Acta med. scandinav.* 162:81, 1958) made a follow-up study of 903 patients who were discharged from Malmö General Hospital after a myocardial infarction. The follow-up group represented 92.7% of those who were discharged home from a total of 1,530 patients hospitalized between 1935 and 1954. These patients were divided into 389 followed for more than five years, 246 followed for two to five years, and 268 followed for two years or less. Of the total series 63% survived a further 5 years, and 40% a further 10 years. If the acute mortality is included, the chance of a 5-year survival at the moment of hospitalization was 39%, and the chance of a 10-year survival was 23%. The survival rate decreases with increasing age at the moment of infarction, but in comparison to sex-age-specific death rates in the population, the prognosis for younger persons was worse than the prognosis for older people. There was a slight general tendency toward a better prognosis for the patients discharged in the latter part of the period investigated. This change was much smaller than the decrease in acute hospital mortality.

There was no obvious sex difference in the material, but in comparison to the sex-age-specific death rates of the population at large, there might be a slightly worse long-term prognosis for women in the ages over 60, which was, however, not statistically significant in the patients reported on. The prognosis for patients with a more severe infarct was not definitely worse than that for those with a mild infarct. Hypertension did not seem to affect the long-term prognosis. Patients with diabetes had a worse long-term prognosis than those without diabetes. Anticoagulant therapy during the acute stage of the infarct did not influence the long-term prognosis, but the interpretation of that finding must be guarded. There was some uncertainty connected with death certification, and while no detailed conclusions were made by the authors, they listed 41.9% dead of subsequent myocardial infarction, 31.9% of coronary heart disease with no evidence of acute myocardial infarction, 6.7% of cerebrovascular diseases, 9.0% of other cardiovascular diseases with 3.7% as malignancy, and 6.7% as miscellaneous for a total of 489 patients for whom such records were available.

Physical Work and Mitral Valvular Disease.—The physical working capacity and its relationships to heart volume, total amount of hemoglobin, and stroke volume was studied in 42 patients with mitral valvular disease, of whom 39 had isolated or predominant mitral stenosis and 3 had isolated or predominant mitral regurgitation. Operation was performed on 27 patients. The physical working capacity, estimated as the work performed continuously at a pulse rate of 170 per minute, was directly correlated to the stroke volume during work. In mitral stenosis the heart volume was large and the working capacity low in relation to the total amount of hemoglobin. A marked enlargement of the heart was usually combined with a high pulmonary vascular resistance. In some patients, however, in whom the pulmonary resistance was almost normal the enlargement might be partly due to left myocardial insufficiency. The degree of incapacity as judged from the exercise tolerance test showed good correlation to the degree of the hemodynamic disturbances. In the patients with mitral regurgitation the heart volume was large but the working capacity normal in relation to the total amount of hemoglobin and the pulmonary vascular resistance was normal, as reported by A. Holmgren and co-workers (*Acta med. scandinav.* 162:99, 1958).

Ulcerative Colitis and Cirrhosis of the Liver.—Ten patients who had ulcerative colitis with coexistent cirrhosis of the liver were reported by Lill Olhagen (*Acta med. scandinav.* 162:143, 1958). In eight, signs of cirrhosis preceded the ulcerative colitis or became manifest so early in the course of the colonic disorder that the condition could not have been the cause of the cirrhosis. Signs of portal hypertension were present in every instance. In view of the disappearance of intestinal symptoms after lienorenal anastomosis in two, it seemed likely that the portal stasis might have caused the ulcerative colitis. Mucosal changes in the colon might be brought about by long-standing venous stasis in the intestine leading to anoxia and impaired nutrition of the mucosa, a mechanism similar to that underlying the formation of varicose ulcers of the leg. No evidence of a causal connection between the two conditions could be shown and until wider experience is gained of operations designed to relieve portal stasis, the presence of ulcerative colitis strengthens rather than weakens the indications for operation.

Physiological Studies of Laborers.—Irma Åstrand (*Acta med. scandinav.* 162:155, 1958) examined 81 truck drivers at rest and during work; 12% had pathological or suspected pathological electrocardiographic tracings at rest and 19% had pathological and 33% suspected pathological tracings during work; 32% had high blood pressure at rest and 47% were considered as overweight. The vital capacity averaged 4.64 liters and the residual volume 1.99 liters or 30% of the total capacity. The ventilation per liter of oxygen intake at submaximal work was about 4 liters higher than for younger persons. The maximal pulmonary ventilation was, however, much lower; 72 of the subjects performed heavy muscular work and of these 2 had cramp-like pains in the precordium as the most troublesome symptom; 20 complained of dyspnea, 31 of local muscular fatigue, 6 of pains in the knee or hip, and the remaining 13 complained of being tired without any specific symptoms. None of the above-mentioned findings were highly correlated with maximal oxygen intake or maximal heart rate. The reason for the decreased physical work capacity could not be explained.

Diabetes and Portal Cirrhosis.—The case records from 108 patients with cirrhosis of the liver (67 men and 41 women) were reviewed by Ragnar Hed (*Acta med. scandinav.* 162:189, 1958) with particular attention to the presence of diabetes. The diagnosis of cirrhosis was verified in all cases at autopsy or by liver biopsy. Chronic alcoholism was present in 55.2% of the men and 4.8% of the women. Primary carcinoma of the liver was present in 20.9% of the men at autopsy and in 4.8% of the women. Diabetes was definitely present in 18 cases (12 men and 6 women). The diabetic incidence was 14.3% in the women and 17.6% in the men. Since these figures were higher than those for diabetes in the entire autopsy material during the same period, a relationship between cirrhosis of the liver and diabetes was assumed to exist. In seven further cases (six men and one woman) the fasting blood sugar level was significantly elevated. If these patients were included, the incidence of impaired sugar metabolism of diabetogenous type becomes 26.5% for the men and 16.7% for the women. The type of diabetes present in this series was comparable to that usually appearing first at from 40 to 60 years of age and occurring most commonly in women. In the present series, however, the diabetic incidence was higher in the men. In explanation of this phenomenon the author suggested that alcoholic cirrhosis was more frequently associated with impairment of carbohydrate metabolism of diabetogenous type than were other forms of cirrhosis.

Carbohydrate Metabolism in Chronic Alcoholism.—A series of 75 male alcoholics was investigated with a view to determining the incidence of disturbances of carbohydrate metabolism by Ragner Hed (*Acta med. scandinav.* 162:195, 1958). In 24 glucose and insulin tolerance tests and liver biopsy were done. Diabetogenous disorders of sugar metabolism were demonstrated in 12 of these, of which 10 showed cirrhosis and 2 a high-grade fatty liver. Four of these 12 patients had manifest diabetes and 8 only diabetogenous glucose tolerance curves. In many of these 8 patients the fasting blood sugar was also pathologically elevated on several occasions. In the intravenous insulin tolerance test relative insulin resistance was demonstrated in all 12. The results of the investigations in these 12 patients indicated a difference in degree only with respect to the diabetogenous sugar metabolism disturbance between the 4 with manifest diabetes and the 8 with only diabetogenous glucose tolerance curves. In 12 patients the glucose tolerance curves were of the nondiabetogenous type. In the intravenous insulin tolerance test the hypoglycemia appeared within the normal interval in all 12 patients. None of these had fully developed cirrhosis. Two types of hypoglycemia were observed—a transient form associated with an alcoholic debauch and a more chronic form. In the present series hypoglycemia was associated with the milder cases of liver degeneration and diabetogenous metabolic disorders in the patients with more pronounced hepatic lesions.

Cardiac Changes in Chronic Alcoholism.—Frederiksen and Hed (*Acta med. scandinav.* 162:203, 1958) made electrocardiograms of 121 male alcoholics aged from 20 to 40 years. In no case was hypertonia, vitium cordis, thyrotoxicosis, or inflammatory cardiac disease present. In 66 the ECG was entirely normal. In 36 the only abnormality was tachycardia above 95 per minute. In 19 others electrocardiographic changes were found as well. Four patients showed auricular fibrillation. In addition, three presented broad, notched P waves, which were also interpreted as due to auricular lesions. It therefore seemed conceivable that the auricle was one of the sites of predilection for cardiac lesions in chronic alcoholism. Isoelectric and diphasic T waves were observed in four and a broad QRS complex in two. Conduction times of only 0.10 occurred in three. Chronic alcoholism was probably the cause of the cardiac lesions in these patients. Whether vitamin B_1 or protein deficiency was the more important factor in causing the cardiac lesions could not be established.

Transfusion Reactions.—A survey was conducted at the St. Erik's Hospital in Stockholm into the incidence of reactions in conjunction with 6,899 transfusions by Olof Ramgren and co-workers (*Acta med. scandinav.* 162:211, 1958). The incidence was 6%. No hemolytic reactions due to serologic incompatibility occurred. The rate for febrile reactions was 3.55%, allergic reactions 1.20%, and other reactions 1.20%. The use of disposable transfusion sets brought down the febrile reaction rate by 50%. The reaction rate increased with the number of previous transfusions. Rouleaux formation in the pretransfusion sample increased the risk of reaction. The age of the blood was of no consequence to the reaction rate if administered within 14 days. If a patient had had a certain type of reaction after blood transfusion, an increased risk of reactions, and of the same type, might be expected on subsequent transfusions.

Thyrotoxic Myopathy and Polymyositis.—Four elderly women, two classified as having thyrotoxic myopathy and two as having polymyositis were described by Boström and Hed (*Acta med. scandinav.* 162:225, 1958). The clinical findings presented great similarities in all four, and were initially misinterpreted as changes due to age. The following facts should be kept in mind for a differential diagnosis between these two forms of myopathy in the older age groups. Thyrotoxicosis often presents few symptoms in elderly patients, and can easily be overlooked; thyrotoxic myopathy is therefore likely to be confused with other forms of myopathy. The basal metabolic rate and urinary excretion of creatine often exhibit pathological values in both myopathies, and therefore have no value in differential diagnosis. In thyrotoxic myopathy, large doses of methylthiouracil produced a marked decrease in creatinuria or its disappearance within about 10 days, and even before any improvement in the muscular weakness had occurred. In polymyositis, this drug had no effect on creatinuria. In thyrotoxic myopathy, the histological changes in the muscle were generally slight, whereas severe damage to the muscle was observed in polymyositis. Progressive muscular weakness in elderly patients, particularly if it is combined with loss of weight, should not be ascribed to the process of aging without a thorough analysis, because certain forms of myopathy are amenable to effective specific or symptomatic therapy.

UNITED KINGDOM

Treatment of Cerebral Neoplasms by Cooling.—General hypothermia for the treatment of malignant growths has been tried but abandoned because prolonged hypothermia can cause cardiac fibrillation. Rowbotham and co-workers (*Lancet* 1:12, 1959) devised a localized form of hypothermia for the treatment of cerebral neoplasms which they used on two patients with glioma and one with astrocytoma after tests had been made on excised human brains. Cooling was effected by a specially designed cannula, used in conjunction with a circulating pump, cooling coil, and circulating fluid reservoir. The cannula consisted of two concentric steel tubes, one for the delivery of cooling fluid and the other for its return to a reservoir. Before reaching the cannula the cooling fluid passed through a coil surrounded by a freezing mixture of solid carbon dioxide and acetone with a temperature of about –74 C. The temperature of the reservoir was kept at about –20 C. Tests on excised brains had shown that insertion of the cooling cannula enabled the temperature of the brain substance to be reduced locally to –20 C. The patients treated were beyond the aid of neurosurgery. Under general anesthesia the brain was exposed and the sterilized cannula inserted into the tumor. It was cooled to –20 C for 20 to 30 minutes. A core of solid frozen brain tissue 10 to 12 mm. in radius formed around the cannula, but brain tissue 2.0 to 2.5 cm. away from the cannula had a temperature of 30 C (86 F). The three patients recovered from the operation. It was shown that it is possible to freeze a local area of the brain without endangering life. One patient died later, another remained the same, and the mental condition of the third patient improved markedly.

Trials with Human Growth Hormone.—A panel appointed by the clinical endocrinology committee of the Medical Research Council investigated the action in man of growth hormone extracted from human pituitaries. Chemically this differs from ox growth hormone, which is inactive in man. Numerous pathologists throughout the United Kingdom cooperated by collecting human pituitaries from fresh cadavers. The acetone-dried glands were extracted with 0.3 M potassium chloride and repeatedly fractionated with alcohol and ammonium sulfate between pH 4.4 and 8.6. The final product was standardized against international standard ox growth hormone. From 10 to 30 mg. of the human growth hormone was given daily to two subjects without pituitary disease and to six with hypopituitarism. From two to eight days later increased nitrogen retention was observed, as shown by a fall in blood urea and urinary nitrogen levels. In addition there was retention of sodium, potassium, magnesium, phosphorus, and sometimes calcium. The amount of potassium, magnesium, and phosphate retained was only what would be anticipated for protein synthesis, calculated from the retention of nitrogen, but the amount of sodium was greatly in excess of this. A consistent rise in fasting blood sugar level was also observed.

Vitamin B_{12} Absorption.—By direct measurement of the distribution of radioactivity in the small intestine of patients given vitamin B_{12} labeled with cobalt-56, Booth and Mollin showed that the site of the absorption of the vitamin in man is the ileum (*Lancet* 1:18, 1959). An oral dose of 1 mcg. of vitamin B_{12} was labeled with 5 μc of Co^{56}. The absorption was studied in patients undergoing laparotomy by examining the distribution of radioactivity in the small intestine three hours after the oral dose was given. An end-window Geiger-Müller counter covered with sterile rubber sheeting and a towel was used to measure the radioactivity. Starting from the duodenojejunal flexure the activity was measured at successive portions of the small intestine down to the ileocecal valve. Absorption was maximum in the distal half or two-thirds of the ileum. This was confirmed by observations on vitamin B_{12} absorption in patients who had undergone resection or short-circuiting of the small intestine. Resection of the jejunum does not interfere with the absorption of the vitamin, but absorption is subnormal if more than about 7 ft. of ileum has been removed. This defect is not corrected by giving tetracyclines. Removal of the ileocecal valve does not interfere with the absorption of vitamin B_{12}. The authors suggested that the physiological absorption of vitamin B_{12} might, in man, be a definite function of the distal part of the small intestine which may contain a specific receptor mechanism for it. A congenital defect of the specific vitamin B_{12} receptor would explain the development of the pernicious anemia syndrome. The authors observed signs of vitamin B_{12} deficiency in patients who had undergone operations on the ileum. The onset of this deficiency was insidious and gradual. They considered that vitamin B_{12} should be given after all operations involving resection of the ileum.

Increase in Myopia.—Herbert Archer, an ophthalmologist of the Birmingham school health service, found more children in schools to be myopic than in previous years. He attributed this to the use and abuse of television. Unless people can be taught to ration the time spent viewing television myopia is likely to become commoner. Archer predicted that a large number of children would pass from the less serious types into the category of high myopia, which is the fourth largest cause of blindness.

Accuracy of Death Certificates.—A study on the accuracy of death certificates was included in the annual statistical review for 1957 (Statistical Review of England and Wales, Her Majesty's Stationery Office, 1958). Over a six-month period 10 large English hospitals arranged for a double death certificate to be issued for every patient dying in the hospital. One certificate was completed by a physician on clinical findings and the other by a pathologist after autopsy. The pathologists agreed with the physicians in 51% of cases, and to this were added another 28% in which the differences were technical rather than actual. Thus in about 80% of the deaths the cause as certified by the physician was confirmed by the pathologist. In 19% the latter found fresh evidence at autopsy that was denied the physician during life. This occurred mainly in the newborn and the aged. Cancer of the lung was underdiagnosed by the physicians, particularly in older patients. Of patients dying from this cause 30% were found to have unsuspected cancers at autopsy. It is evident that the death rate from cancer of the lung in Britain is even higher than it is reported to be. There was also disagreement between physicians and pathologists on the diagnosis of arteriosclerotic and coronary heart disease. They agreed on only 41% of cases, which corresponded closely to the 44% accuracy rate for myocardial infarction found by Paton at the Edinburgh Royal Infirmary. A number of cases mistaken for coronary disease by the physicians were in fact pulmonary embolism.

Carbon Monoxide Poisoning.—Recommendations made by the Medical Research Council (MRC) on the treatment of carbon monoxide poisoning have undergone revision. Three years ago the MRC issued a report stating that a carbon dioxide-oxygen mixture should not be used for the resuscitation of persons poisoned by carbon monoxide. The reason given at the time was that under the uncontrolled conditions of first-aid, carbon dioxide might accumulate to dangerous levels in the tissues. This argument was seriously challenged by experts in so far as carbon monoxide poisoning was concerned, on the grounds that the administration of an oxygen-carbon dioxide mixture increased the elimination of carbon monoxide and brought about a more rapid recovery. A special subcommittee was therefore set up by the MRC to consider the problem. As a result of experiments on animals and on human volunteers poisoned with carbon monoxide, it was concluded that the administration of a mixture of oxygen and carbon dioxide leads to a more rapid elimination of carbon monoxide from the blood than does oxygen alone. From this and clinical evidence the MRC subcommittee considers that on balance a mixture of 5% carbon dioxide in oxygen is more likely to facilitate recovery from carbon monoxide poisoning than oxygen alone, but that there is no advantage in increasing the amount of carbon dioxide beyond 5%.

Pleuropneumonia-like Organisms in Genital Infections.—Further evidence for the role of pleuropneumonia-like organisms (PPLO) in pathological conditions, particularly in nongonococcal urethritis (NGU) in men, was obtained by Klieneberger-Nobel (*Brit. M. J.* 1:19, 1959). The identification of these organisms is difficult as they can be detected only by culture. Electron microscopy was abandoned as a means of identification, as the appearances could not be correlated with cultural methods. Urine specimens and discharge or scrapings from the urethra were obtained from men with NGU and related conditions, and from the vagina, cervix, or urethra of women from venereal, gynecologic, and prenatal clinics. Patients with Reiter's syndrome and a number of partners of patients from venereal disease clinics were also examined. The sediment from urine specimens was used for culture. PPLO were found to be absent from the urine of 97% of healthy men examined. One had NGU and another was a symptomless carrier of the organisms. PPLO were completely absent from the urine of 43 prepuberal boys seen in the medical wards of a hospital. The discharges and scrapings from men from the venereal disease clinics were positive for PPLO in 25% of 201 patients. The highest number of positive results (48%) was obtained in those that had recently acquired NGU; 30% of the men with gonorrhea harbored PPLO. The organisms were present in the scrapings of 10% of the patients with Reiter's syndrome.

The incidence of PPLO was found to be much higher in the women patients; 56% of those attending venereal disease clinics were infected. In those with gonorrhea, whether treated with penicillin or not, nearly 90% carried the organisms in the urethra, vagina, or cervix. Surprisingly enough 23.5% of the pregnant women examined harbored PPLO in the cervix. The incidence in gynecologic patients of a London hospital was 17%. PPLO were not found in the synovial fluid of patients with Reiter's syndrome, and only rarely in the urethral discharge. This refutes the commonly held view that Reiter's syndrome and NGU have a common cause. The author's observations show that genital strains of PPLO are absent before puberty, and rare in healthy young men and women. They are associated with recently acquired urethritis in a high proportion of men suffering from NGU, and with cervicitis, vaginitis, and urethritis in women. They are often present in patients with gonococcic and trichomonal infections and are particularly likely to be transferred by sexual intercourse.

Spirochetal Rat Bite Fever.—Rat bite fever caused by infection with Spirillum minus is extremely rare in England, no case having been reported for over 30 years. Edmunds and Tilley described a case occurring in Edinburgh due to a mouse bite (*Lancet* 2:1211, 1958). No reference to mice as a source of infection in this country has been reported before. An 11-year-old boy was bitten by a mouse and one week later developed a severe headache and pyrexia. Two weeks after the bite the puncture marks were painful, swollen, and red, and large spots appeared on the backs of his arms and legs. The pyrexia persisted, with intermittent fever around 103 F. The conjunctivas were injected, the eyelids were swollen, and the patient had an intractable headache. Appetite and weight loss occurred and a moderate soft enlargement of the principal lymph nodes was noted. The presence of Sp. minus was demonstrated by inoculation of mice and guinea pigs with the boy's blood. Large doses of penicillin were given. Although there is a widespread belief that mice are harmless, the risk to those handling them in the laboratory and during disinfestation should be more generally known.

Oral Treatment of Ringworm.—It was shown by Gentles that guinea pigs experimentally infected with Microsporon canis and Trichophyton mentagrophytes quickly responded to small oral doses of the antibiotic griseofulvin, which was isolated from Penicillium griseofulvum (*Nature* 182:476, 1958). The antibiotic is evidently absorbed and secreted into the dermis, as it was found by Gentles in the hair of treated animals. Williams and co-workers gave the antibiotic in oral doses of 0.5 Gm. four times a day to nine patients with clinical Trichophyton rubrum infection of the skin or nails and one with Microsporon audouini infection of the scalp (*Lancet* 2:1212, 1958). No local treatment was given. The antibiotic caused rapid relief of itching, growth of infected nails, loss of hyperkeratosis, and disappearance of the fungus from nail scrapings. In the one patient with ringworm of the scalp, the hair did not fluoresce under Wood's light three weeks after beginning treatment. The toxicity of griseofulvin is low and no side-effects were observed. These preliminary results support the hope that griseofulvin may be of use in the oral treatment of ringworm.

Surplus Women Declining.—For many years there have been more women than men in Britain. If the present trend continues and there are no more wars there will soon be as many men as women, according to the Registrar General's report, which states that the long-continued increase in the ratio of women to men, which started in 1821, or earlier, has now ended. In the last century, although from 40 to 50 more boys were born for every 1,000 girls, there was an excess of females over males because of the higher death rates for boys. About 60 more boys are now born for every 1,000 girls, but the death rate of boys is falling. At the last census women were still in the majority—1,082 to every 1,000 men. The report states that divorced women outnumber divorced men 130,000 to 79,000, because more men than women marry again. There are 2,319,000 widows, but only 739,000 widowers. This is attributed to the fact that women, particularly married women, live longer than men.

Antibiotics and the Common Cold.—In a letter to the *Lancet* Professor Garrod deprecates the use of chloramphenicol and other antibiotics, which have recently been recommended for the prevention of complications, in the treatment of the common cold. His chief reason for proscribing chloramphenicol is because it is known to cause bone marrow damage, and therefore its use is unjustified for trivial purposes. If an antibiotic must be used for the treatment of colds it should be penicillin, which is cheaper, safer, and can be used in the form of a spray, snuff, or pastille, but Garrod objects even to this form of treatment as it may lead to sensitization. If all common colds were generally treated by antibiotics it would add $315,000,000 to the annual drug bill of the nation.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Periarteritis Nodosa: Review. P. Bro-Rasmussen. Ugesk. laeger 120:1481-1489 (Nov. 6) 1958 (In Danish) [Copenhagen].

During the last 10 years 17 patients with periarteritis nodosa were admitted in the Rigshospitalet in Copenhagen. Of the 9 patients in whom diagnosis was made during life, 7 are living from 6 months to 9 years after the diagnosis. Periarteritis nodosa is counted among the collagen diseases, which also include chronic polyarthritis, lupus erythematosus disseminatus, thrombotic thrombocytopenic purpura, scleroderma, polymyositis, and dermatomyositis. Morphologically, all are characterized by marked changes in the connective tissue. Periarteritis nodosa occurs most frequently between the ages of 20 and 40 years and is seen more often in men than in women. The picture is polymorphic. Long-continued fluctuating fever is the main symptom. The frequency of admissions and the number of diagnoses made in life support the concept that the disease is increasing in frequency. Periarteritis nodosa should be considered in unusual combination of symptoms and in vague progressive cases, with fever, muscular asthenia, and loss of weight. The diagnosis is supported by information on allergic manifestations, hypersedimentation, hypergammaglobulinemia, transient electrocardiographic changes, and transient roentgenologic pulmonary changes. Only skin and muscle biopsies afford certain diagnosis. The treatment consists of the administration of 11-oxysteroids and is otherwise symptomatic. The prognosis is unfavorable. There seems, however, to be a tendency to remission in most cases in which the viscera are not involved. The disease may have an acute course with fatal outcome; the course may also be insidious and protracted or show remissions and acerbations with increasing symptoms of ischemic lesions of the different organs.

Negative L. E.-Cell Phenomenon in True Systemic Lupus Erythematosus. P. Formijne and F. van Soeren. Lancet 2:1206-1207 (Dec. 6) 1958 [London].

The authors report on a 53-year-old man with the typical aspect of systemic lupus erythematosus, in whom the L. E.-cell test gave completely negative results. Further immunological investigation showed that the Wassermann test could not be *carried out, owing to anticomplementary activity* of the patient's serum. It was then considered that a connection might exist between this activity and the negative L. E.-cell phenomenon. When excess normal fresh human complement was added to the patient's serum, the L. E.-cell phenomenon became clearly positive. Positive L. E. serum was heated at 56 C (132.8 F) for between 30 and 60 minutes. Fresh leukocytes washed in sodium chloride solution and fresh leukocyte nuclei washed in sodium chloride solution gave negative results with this inactivated serum concerning the L. E.-cell phenomenon; after addition of fresh human or guinea pig serum, a few rosettes and a few classic L. E. cells were found. The patient's condition deteriorated, and he died in cardiac failure. The diagnosis of systemic lupus erythematosus was confirmed by autopsy.

Free-acting complement plays an important role in the production of the L. E.-cell phenomenon. Inactivation of a positive L. E. serum by heating is possible, when it is used with washed leukocytes and washed leukocyte nuclei. After addition of human or guinea pig complement to this system, a weakly positive L. E.-cell phenomenon reappears. The L. E.-cell phenomenon can be negative, notwithstanding the presence in the serum of the specific L. E. factor and of complement, if complement-inhibiting substances are also present. In this case the L. E.-cell phenomenon can be demonstrated by the addition of fresh complement. The L. E.-cell phenomenon may perhaps be inhibited by lack of complement.

Metastasizing Carcinoid. L. Heilmeyer and R. Clotten. German M. Month. 3:338-340 (Nov.) 1958 (In English) [Stuttgart, Germany].

The authors report on a 56-year-old man with metastasizing carcinoid of the small intestine, whose case was peculiar with regard to its clinical aspects and metabolic behavior. The clinical course of the disease was more severely malignant than usual, with a greatly enlarged liver, the surface of which

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The place of publication of the periodicals appears in brackets preceding each abstract.

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showed numerous nodules varying from the size of a pea to that of an apple. There were bouts of high fever, and the erythrocyte sedimentation rate was considerably increased. Flushes occurred very frequently and were particularly severe. Oliguria and tachycardia were present in the absence of fever. In contrast to these findings, the intermittently normal excretion of hydroxyindolacetic acid and the increased excretion of tryptophan in the urine were surprising and difficult to interpret. Another substance which gave the same color reactions as hydroxyindolacetic acid also was observed; it might have been hydroxyindolacetaldehyde, another intermediate-stage decomposition product during the oxidation of 5-hydroxytryptamine to hydroxyindolacetic acid, or the gluconate of this acid. Other tryptophan derivatives were present in the electrophoretic pattern of the urine. A particularly severe flush was observed after 2 intravenous injections, each containing 50 mg. of 5-hydroxyindolacetic acid; the excretion of hydroxyindolacetic acid in the urine was simultaneously increased, and 38.3 and 35.1 mg. of the administered amounts was recovered from the urine within 24 hours. A severe flush also was observed after the intramuscular administration of 2.5 mg. of reserpine.

A possible explanation for the puzzling normal excretion of 5-hydroxyindolacetic acid and the increased tryptophan excretion is suggested as follows. A loss of the enzymes, which contribute to the oxidative transformation of 5-hydroxytryptamine into 5-hydroxyindolacetic acid, may result from the dedifferentiation of the carcinoid cells; 5-hydroxytryptamine may then accumulate in the cells, and finally a retransformation in tryptophan and hydroxytryptophan, respectively, may occur, which cannot be distinguished with the techniques used. Though not verified, this concept seems plausible. Another explanation would be that the clinical manifestations in this patient were not elicited by hydroxytryptamine but by another tryptophan derivative. Clinically the conclusion is inescapable that extensive carcinoid metastases may be associated with a normal excretion of hydroxyindolacetic acid in the urine. In such cases simultaneous determination of tryptophan excretion may be of diagnostic value.

Diagnostic Value of Needle Biopsy of the Liver. A. Lattanzi and U. Urbano. Omnia med. 36:185-209 (May-Aug.) 1958 (In Italian) [Pisa, Italy].

Specimens of the liver were obtained by needle biopsy from 53 hospitalized patients. Primary or secondary neoplastic disease was present in 17 patients, subacute or chronic hepatitis with progression toward sclerosis in 17, cirrhosis of the liver in 14, systemic blood disease in 2, and reticuloendotheliosis in 1. Needle biopsy of the liver was the main diagnostic procedure in 21 patients; it contributed to the formulation of the diagnosis in 25; it had insignificant diagnostic value in 5; and it gave an erroneous response in 2. Of the 14 patients with cirrhosis of the liver, needle biopsy of the liver established the diagnosis in 5 patients; it confirmed a previously established diagnosis by clinical means and laboratory findings in 8; and it gave disagreement with the clinical picture in 1 [It seems that the specimen of the last patient was obtained from the intact part of the liver.] Needle biopsy of the liver is particularly useful for an early diagnosis in cirrhosis of the liver.

Of the patients with subacute or chronic liver disease, needle biopsy of the liver was the main diagnostic means in 7 patients; it confirmed a previously established diagnosis in 7; and it was of insignificant diagnostic value in 2. Needle biopsy of the liver in subacute or chronic liver disease may also have a prognostic value; it can aid in detecting a latent sclerotic progression at a stage when the disease appears to be clinically cured. Of the 17 patients with primary or secondary neoplastic disease, needle biopsy of the liver was the main diagnostic means in 10 patients; it confirmed a previously established diagnosis in 4; it was of insignificant diagnostic value in 2; and it gave a discordant response with other procedures in 1. Needle biopsy of the liver in patients with neoplastic disease was supported and guided by the findings of laparotomy. The authors conclude that needle biopsy is an innocuous and fairly reliable diagnostic procedure for the establishment of the histological picture of various hepatic diseases and that it seems to be superior to other laboratory methods.

The Role of Hemodialysis (Artificial Kidney) in Acute Poisoning. G. E. Schreiner. A. M. A. Arch. Int. Med. 102:896-913 (Dec.) 1958 [Chicago].

The role of the artificial kidney in human poisoning may be considered from 2 points of view: the removal of (1) dialyzable poisons and (2) nephrotoxic poisons; the latter produce damage to the kidneys and are not different from other causes of acute renal insufficiency. In some instances, general toxicity may be produced from the poison itself, while in others it is a produce of the uremic syndrome. The effective use of hemodialysis is based on the following assumptions: 1. The poison molecule can diffuse through cellophane from plasma water and has a reasonable removal rate, or dialysance. 2. The poison is distributed in accessible body-fluid compartments. If substantial fractions of the absorbed poison dosage are bound to protein molecules, concentrated in important fluid compartments (e. g., cerebrospinal fluid), or attain a significant intracellular concentration, then effective dialysis will be sharply limited. This restriction is diminished, however, if the "loculated" portion is in diffusion or chemical equilibrium with a significant moiety in the plasma water. 3. There is a relationship between toxicity and the blood concentration and duration of the body's exposure to this circulating poison. 4. The amount of poison dialyzed constitutes a significant addition to the normal body mechanisms for dealing with the particular poison.

Many types of acute poisons are not susceptible to hemodialysis when measured against these considerations. Anticholinesterase compounds, as an extreme example, act much too rapidly for a favorable relationship between blood level and clinical toxicity. The same is probably true of the tissue necrosis due to the phosphorus content of rat-paste and matchstick poisoning.

The author is concerned with poisons for which removal by dialysis has been demonstrated by chemical measurement or reversal of clinical state. These include various barbiturates and salicylates, bromide, thiocyanate, ammonia, strontium, radiocalcium (Ca^{45}), tritium, and glutethimide. The author reviews the role of hemodialysis in the study and treatment of acute poisoning on the basis of 8 years' experience embracing 24 patients with dialyzable poisons and 15 patients with nephrotoxic injury. Survival rates were 83 and 47%. Barbiturate, salicylate, bromide, glutethimide (Doriden), and diphenylhydantoin (Dilantin) poisoning are reviewed in detail, with illustrative case histories appended. The first known instance of successful dialysis of severe methyl salicylate poisoning is presented, with reduction in blood salicylate level from 110 to 29 mg. per 100 cc. Early dialysis is suggested to abort the full clinical picture from dialyzable poisons and nephrotoxic injury.

Treatment of Chronic Asthma with Prednisolone: Significance of Eosinophils in the Sputum. H. M. Brown. Lancet 2:1245-1247 (Dec. 13) 1958 [London].

The subcommittee on clinical trials in asthma of the British Medical Research Council in 1956 had found no real advantage in cortisone acetate treatment of chronic asthma, compared with bronchodilator drugs. Analysis suggested that its methods were not beyond criticism; so general practitioners in the Derby area were asked to refer chronic asthmatic patients to the chest clinic to take part in another trial with prednisolone. This included patients who were already receiving steroid therapy, as well as those who joined the trial later. There were 90 patients in all. The trial was limited to patients who had had chronic bronchospasm for at least a year, and who had proved refractory to all other forms of treatment over at least one month. Early in the trial it was found that the distinction between asthma and chronic bronchitis with predominant bronchospasm was difficult.

The discovery of eosinophilic sputum in patients who responded dramatically to prednisolone prompted the improvisation of a method of examining the sputum and made it possible to separate the true asthmatics with eosinophilic sputum from the others. The success of this method suggested the examination of the sputum of patients receiving prednisolone. Corticosteroids clear the blood of eosinophils, but it was found that this did not happen in the sputum. Eosinophils in large numbers in the sputum were associated with a good response to prednisolone, and few or no eosinophils with a poor response.

Except when bronchospasm was very severe, the dose given was 5 mg. thrice daily for a week, followed by reassessment and adjustment of dose. All patients were given notes warning them of the dangers involved in prednisolone therapy. As a further safeguard, notes on the dangers of treatment were issued to family physicians. Each patient was told to take as little prednisolone as possible to keep him from wheezing. When wheezing had ceased for a few days, the dose was reduced by 2.5 mg. every 3 days until wheezing returned slightly. It should then be increased by 2.5 mg., so that wheezing disappeared again, and then continued at that level for about 10 days, when a further attempt should be made to reduce the dose. Thus, the patient was constantly trying to reduce the dose and finally stop treatment. Often patients were too enthusiastic in reducing dosage, so that spasm got out of hand and 15 mg. a day was needed for a week or so to control it. With these methods and by careful supervision and the use of antibiotics when needed, the risk of side-effects and complications was minimized. The screening technique for eosinophils in the sputum is described.

In some patients treatment with prednisolone had to be continued for a long time. Which is the lesser evil, disabling asthma or the dangers of long-term prednisolone treatment? All patients who had to make this choice chose to continue treatment. The elderly bronchitic patient with severe bronchospasm rarely benefited. Younger patients who obtained complete relief from bronchospasm usually had little or no residual dyspnea once the bronchospasm had disappeared. On the other hand, older asthmatics in whom emphysema had developed were still dyspneic. Experience showed that, if there was no improvement within 2 weeks on 15 or 20 mg. of prednisolone per day in the absence of purulent sputum, no significant benefit would be derived from continuing treatment. Prednisolone was used in children only when antispasmodics were of no avail, when there was emphysema and a poor prognosis, when the child had constant bronchospasm punctuated by exacerbations, and after eosinophils had been demonstrated in the sputum. Though prednisolone is effective in suitable cases, it never does more than suppress the asthmatic state, and it does not abolish eosinophils in the sputum, though the quantity is much reduced.

Value of Thyrotropin Stimulation Test in Diagnosis of Myxedema. T. Friis, L. K. Christensen and M. S. Andersen. Ugesk. laeger **120**:1545-1548 (Nov. 20) 1958 (In Danish) [Copenhagen].

Investigations confirm that thyrogenic myxedema in patients given thyroidin preparations can be excluded if the patients react to thyroid-stimulating hormone (TSH) with fairly normal absorption of radioiodine (I^{131}) in the thyroid gland. TSH tests with 4 U.S.P. units of TSH were carried out in 33 patients treated with thyroidin. Eleven had thyrogenic myxedema; they did not react to TSH with increased absorption of I^{131}. Of the 22 patients who presumably did not have myxedema at the start of treatment, 6 did not react to TSH; the thyroid gland is thought to have undergone atrophy in these cases as a result of thyroidin treatment.

Ammonia Intoxication Treated by Hemodialysis. J. E. Kiley, J. C. Pender, H. F. Welch and C. S. Welch. New England J. Med. **259**:1156-1161 (Dec. 11) 1958 [Boston].

Increased concentration of ammonia has been observed in many patients with hepatic coma. On the basis of investigations to determine whether ammonia present in the blood could be removed by a Kolff type of artificial kidney, the authors reported in 1955 that ammonia was removed by an artificial kidney with a dialysance varying from 50 to 80 ml. per minute when blood flow was 100 ml. per minute and membrane area was 12,000 sq. cm. They now report the application of hemodialysis to 5 patients who were comatose with ammonia intoxication. All these patients had advanced liver disease and lapsed into coma, with elevated blood ammonia levels, after massive gastrointestinal hemorrhage. All had ascites, and the prognosis was considered sufficiently poor to warrant trial of a new treatment. All were treated by esophageal tamponade, gastric lavage, and catharsis. A modified Kolff rotating-drum type of artificial kidney was used.

Three patients were treated by dialysis in the hope of relieving overwhelming ammonia intoxication of the exogenous type. No untoward effect of dialysis was observed. The first 2 patients came out of coma after the dialysis. Dialysis in the third patient was too limited by ordinary standards (only 11 liters of blood ran through the artificial kidney) to be of much therapeutic significance. This patient did not regain consciousness and died 2 days after the dialysis was terminated at a time when the first 2 patients were again alert and rational. In these 3 patients ammonia intoxication was not associated with any other biochemical disorder of comparable significance. In the other 2 patients severe ammonia intoxication was associated with other biochemical abnormalities. In each of these last 2 patients dialysis removed large amounts of ammonia nitrogen and other nonprotein-nitrogen constituents of the blood. In one of these 2 patients the temporary improvement noted was dramatic. Thus, 4 of 5 patients showed clinical improvement after effective dialysis. In the patient who died, dialysis was ineffective because of blood clotting. The authors conclude that ammonia may be removed by hemodialysis from patients suffering from ammonia intoxication, and that removal of ammonia by dialysis may be beneficial.

Microlithiasis of Pulmonary Alveoli. D. Hojman, R. B. Podio and O. C. Barreiro. Rev. Asoc. méd. argent. **72**:411-417 (Oct.) 1958 (In Spanish) [Buenos Aires].

Microlithiasis of the pulmonary alveoli is a rare familial and congenital disease of unknown origin. The disease consists of absorption of calcium salts by the lung parenchyma and the formation of microliths of various sizes, which occupy the pulmonary alveoli in innumerable quantities. The disease follows its course without symptoms or in presence of mild dyspnea for several years. It causes chronic cor pulmonale and insufficiency of the heart. It can be detected by chance during a routine roentgenologic examination of the chest. The roentgenograms of the chest are characteristic, showing complete bilateral opacification of the lungs, which involves the whole structure with the exception of the apex. The respiratory symptoms reported by the patients, as well as those heard on auscultation of the chest, are out of proportion to the extensive lesions of the lungs, as shown in the roentgenograms. Of the total 44 cases reported in the literature, an autopsy was performed in 12 cases, and a biopsy in 11. The pulmonary disease is restricted to the pulmonary parenchyma, the pulmonary alveoli, and the consequent pulmonary heart. All other organs and structures are normal. The microliths are free within the alveoli, the walls of which are normal and in rare cases involved by fibrosis. On touch, the lung gives the sensation of being a pumice stone. Blood vessels, bronchi, and pleura of the involved lungs are normal. If the lung tissue is put in water, it sinks. On cutting, it cracks like cutting metal. The cutting surface looks as if it were sandpaper.

A man, 58 years old, reported for consultation with symptoms of insufficiency of the heart. He had had moderate dyspnea for 18 or 20 years. Clinical examination showed a chronic pulmonary heart and very mild respiratory disorders detected on auscultation of the chest. The roentgenograms of the chest were typical of microlithiasis of the pulmonary alveoli. All other organs and structures were normal. It was learned that 2 brothers of the patient had died of the same disease and that his 5-year-old son apparently had the same disease in an early stage. Prior to death the patient was given a diagnosis of microlithiasis of the pulmonary alveoli. Partial autopsy with histological studies of tissues from the lower lobe of a lung confirmed the clinical diagnosis.

Mild and Severe Varieties of Erythema Multiforme Exudativum: Observation of Several Cases. G. Manganelli. Gior. clin. med. 39:1327-1353 (Sept.) 1958 (In Italian) [Bologna, Italy].

The author reports on 15 patients with erythema multiforme exudativum, 7 of whom had the mild variety, 4 the severe variety, and 4 the intermediate variety of the disease. In addition to the conventional symptoms, the patients with the mild variety developed high fever. The patients with the severe variety, also known as the Stevens-Johnson syndrome, manifested some, but not all, of the common features of this syndrome, which ran a fatal course in 2 patients. The intermediate variety was characterized by mild symptoms with involvement of the gastrointestinal tract in all 4 patients and an affection of the kidneys in 3. The renal lesions appeared during the resolutive phase of the disease and persisted for a certain period of time after diarrhea, vomiting, and cutaneous lesions had subsided.

The author concludes that in this series the mild and the severe varieties of erythema multiforme exudativum appeared to be facets of the same disease, because some of the symptoms which were not apparent in one were present in the other. Involvement of the viscera developed in both varities, and a higher erythrocyte sedimentation rate was observed in both. The Stevens-Johnson syndrome seemed to represent only one form of erythema multiforme exudativum. The clinical features of erythema multiforme exudativum in some of these patients were similar to those of the collagen diseases. Among these were a precarious state of health, arthralgic pain, and cutaneous erythema.

The Incidence of Peptic Ulceration in Some African Tribal Groups. A. B. Raper. Tr. Roy. Soc. Trop. Med. & Hyg. 52:535-546 (Nov.) 1958 [London].

The incidence of gastric and duodenal ulcer in 3 groups of people of diverse origins, living in the neighborhood of Kampala, Uganda, was assessed by means of a consecutive series of postmortem examinations. For male subjects, the gross incidence of peptic ulcer in the local people was 13.68%, in Nilotic immigrants 5.4%, and in immigrants from the southwest (especially Ruanda) 20.6%. The generally high incidence, 15.3% in men and 4.65% in women, is in contradiction of previous reports from tropical Africa. It is suggested that the causes of peptic ulcer are abundantly operative in tropical Africa but that the conditions in which the disease may be brought to notice are rarely fulfilled.

The results of this survey give confirmation to the view that peptic ulcer is commoner in immigrants from the southwest than in the people of central Uganda, but it was an unexpected finding that another group of immigrants, the Nilotics, should show a lower incidence than the local people. The author feels that it is not necessary to postulate variations in "racial" susceptibility to ulcer, at least as the immediate cause, for in the population from which these data are drawn the 3 groups are exposed to very different conditions of life. The immigrants from the southwest represent the section of the community subject to the greatest stress; their life is the hardest, their food the poorest, often long intervals elapse between their meals, the prevalence of disease is greatest among them, and fears for the future must be constantly present in their minds. These considerations offer an entirely adequate explanation for any proneness to ulcer that they may exhibit. They certainly offer a marked contrast to the Nilotic immigrants, in whom the lower incidence of ulcer could well be related to the fact that these people are better fed and have a more carefree attitude toward life, a consequence partly of their greater efficiency as wage earners. The local people occupy in these respects a position intermediate between the 2 immigrant groups. Thus, if any influence is to be attached to innate susceptibility to ulcer, it depends in these 3 groups on the success with which they face the complexities of life, and thereby encourage or impede the action of the well-recognized etiological agents of peptic ulcer.

Intestinal Polyposis and Mucocutaneous Pigmentation (Peutz-Jeghers Syndrome): Further Comments and Report of an Additional Case. L. C. Bartholomew and D. C. Dahlin. Minnesota Med. 41:848-852 (Dec.) 1958 [St. Paul].

The authors point out that an earlier report from the Mayo Clinic on intestinal polyposis and mucocutaneous pigmentation (Peutz-Jeghers syndrome) described 6 new cases and reviewed 69 cases reported in the literature to the end of 1955. Since then a sufficient number of additional cases have been presented to justify further reflections on this disease, particularly on the potentially malignant character of the polyps. The authors present the history of an 82-year-old man, who in addition to urinary retention had experienced a severe substernal pain, and in whom an electrocardiogram showed the typical findings of an acute anteroseptal myocardial infarction. The patient died 6 hours later. Postmortem examination revealed coronary sclerosis, a recent infarct in the apex and anterior wall of the left ventricle with rupture of the myocardium into the pericardium, benign prostatic hypertrophy, and bilateral hydronephrosis. An incidental finding was that of single polyp, 1 cm. in diameter, in the fundus of the stomach and 6 polyps in the colon. The examiner's awareness of the aspects of the Peutz-Jeghers syndrome led to a search for, and the demonstration of, the characteristic pigment on the mucosa of the lips. Microscopically, all the polyps were benign.

In the 2 years that have elapsed since the earlier review of 75 cases, 42 additional cases of this syndrome came to the authors' attention, bringing the total to 117. The pigment was present on the lips in 115 of the 117 patients, thus making this the single most important physical sign. It was noted on the buccal mucosa in 103 of the 117 patients. The polyps were present in some part of the small intestine in 108 of the 117 patients. The exceptions included 7 patients with polyps in the rectum alone, 1 with polyps in the colon and stomach, and 1 with polyps in the rectum, colon, and stomach. Episodes of abdominal pain and some form of gastrointestinal bleeding were the major symptoms. Recurrent attacks of colicky abdominal pain occurred in 99 of the 117 patients. About 55% of the patients have some evidence of the familial nature of this disease.

The major aspect of this syndrome that remains debatable pertains to the potential malignant nature of the polyps. The peculiar histological characteristics of the polyps that the authors were able to study led to the suggestion that these tissue excrescences represent a developmental abnomality rather than true adenomatous polyps. The 3 predominant types of cells of the normal mucosa of the small intestine, namely, columnar absorbing cells, goblet cells, and coarsely granular Paneth cells, were found within the jejunal and ileal polyps that were studied in 5 patients. The authors feel that the over-all pattern of these polyps strongly suggests that they are the result of a growth disturbance similar to that which produces hamartomas of the lungs. None of the polyps which they studied in the Peutz-Jeghers syndrome appeared malignant or even premalignant. However, although the colonic and rectal polyps studied in patients with the Peutz-Jeghers syndrome have appeared benign, there is no evidence to suggest that these patients are immune to the development of ordinary adenomatous polyps and carcinomas in these locations.

Intolerance for Gluten in a Patient with Regional Ileitis. J. R. Chan Jon Chu. Nederl. tijdschr. geneesk. 102:2150-2154 (Nov. 1) 1958 (In Dutch) [Amsterdam].

The author presents the history of a 26-year-old woman who for nearly a year had been troubled with abdominal pains and constipation. After a more severe attack of pain accompanied by vomiting, diarrhea developed, which persisted. There were 3 or 4 loose or watery stools daily. Loss of weight resulted. "Chronic appendicitis" and later tuberculous peritonitis were suggested. Diarrhea and weight loss continued despite conservative treatment. Regional ileitis was diagnosed at laparotomy, and an ileocecal resection was performed. Twenty months later, at a second operation for regional ileitis, the lower third of the remaining small intestine was resected. Abdominal pains, diarrhea, and loss of weight recurred after both operations, and after the second operation the diarrhea gradually became more severe, and symptoms of malabsorption developed. Fat balance studies revealed extreme steatorrhea. The patient was treated with a gluten-free diet; prompt improvement followed, and the fat absorption rose. The gluten-free diet combined with up to 25 mg. of prednisone daily effected no increase in fat absorption. Treatment with gluten-free diet alone resulted in complete clinical recovery.

Angiographic, Functional and Clinical Aspects of Obliterating Arteriopathy of the Lower Extremity and Their Relationship. V. Uberti and G. Japichino. Omnia med. 36:130-183 (May-Aug.) 1958 (In Italian) [Pisa, Italy].

The authors investigated the correlation between morphologic, functional, and clinical aspects of occlusion at various sites of an affected artery in 487 patients with arterial occlusion of the lower extremity. Obstruction of the superficial femoral artery was present in 112 patients (22.4%); it was related to atherosclerosis in 106 patients and to thromboangiosis in 6. Peripheral blood flow was in most instances fairly adequate in relation to the collateral circulation. Intermittent claudication developed in 104 instances, pain at rest in 17, cyanosis in 14, and ulcer in 4. Occlusion of the popliteal artery was present in 19 patients (3.8%); it was related to atherosclerosis in 11 patients and to thromboangiosis in 8. Digital plethysmography revealed that peripheral blood flow was more pronounced in patients with occlusion of the popliteal artery than in those with occlusion of the superficial femoral artery. Clinical symptoms were also more marked; intermittent claudication affected all patients; trophic lesions and pain at rest were also more intense.

Occlusion of the femoral-popliteal tract developed in 23 patients. The occlusion was severe, and plethysmograms showed considerable reduction in peripheral blood flow. Severe clinical symptoms were directly related to the reduced peripheral blood flow. Occlusion of the anterior tibial artery was present in 21 patients. Plethysmograms showed variations from extreme reduction to almost normal pattern in peripheral blood flow. Many instances of severe ischemia were observed: pain at rest in 12 patients, hypothermia in 10, and cyanosis in 12. Occlusion of the posterior tibial artery was present in 27 patients. Total occlusion was more frequent than partial occlusion. Plethysmographic patterns showed a considerable decrease in peripheral blood flow at rest and a marked increase after reflex vasodilation. Multiple occlusions of the arteries of the leg, which were mostly related to thromboangiosis, were observed in 116 patients (23.2%). Plethysmograms showed a considerable decrease in peripheral blood flow. The main clinical feature was a rapid development of ischemia. Associated occlusions of the arteries of the thigh and the leg were present in 67 patients. Reduction in peripheral blood flow was considerable and was often very high. Intermittent claudication, pain at rest, and necrotic lesions were frequent and severe.

The clinical symptoms related to arterial occlusion in patients of this series were often worse than those usually observed at corresponding sites of obliterated arteries of the lower extremity. The succession of clinical symptoms reflected the gradual development and the extent of arterial lesions.

Kahler's Disease and Proteinuria. J. Warter, P. Métais and J.-M. Mantz. Semaine hôp. Paris 34:2919-2930 (Dec. 4) 1958 (In French) [Paris].

The authors studied the incidence of proteinuria in 16 patients with multiple myeloma (Kahler's disease). Renal manifestations generally appeared simultaneously with pathological changes in the bones, but in one patient the occurrence of anuria led to the diagnosis of multiple myeloma. Proteinuria was manifested in one patient several months and in another patient 4 years before other symptoms and signs of multiple myeloma appeared. The filter-paper electrophoresis of urine from patients with proteinuria revealed more often a mobility of gamma globulins, and more rarely of beta globulins, with or without a corresponding serum globulin peak. Thus, in 3 of the 16 patients globulinuria was the initial symptom and the premonitory sign revealing multiple myeloma. The diagnostic value and prognostic significance of electrophoretic analysis of urine are emphasized, particularly in patients with severe proteinuria of unknown origin.

The various physicochemical aspects of Bence Jones proteins are considered, such as their thermal solubility, their electrophoretic pattern, and their amino acid composition. The problems regarding the origin of Bence Jones proteins, their release into the circulation, and their rapid excretion through the kidneys due to their low molecular weight (about 44.000) are discussed. Nitrogen metabolism was studied in patients with multiple myeloma by evaluating the intestinal absorption of methionine and of glycine labeled with radio carbon (C^{14}). The intensity of protein synthesis, which characterizes myeloma, entails an indubitable state of nitrogen deficiency. The hyperabsorption of the amino acid administered in such cases seems to be a manifestation of this deficiency.

The Clinical Significance of Diverticulosis. R. S. Boles Jr. and S. M. Jordan. Gastroenterology 35:579-582 (Dec.) 1958 [Baltimore].

The authors report on 134 men and 160 women with diverticulosis, who were studied at the Lahey Clinic in Boston. The average age of the patients was 55 years. One hundred nineteen patients (40%) had a history of definite laxative abuse, and 33 patients (11%) complained chiefly of diarrhea. The medical management of the patients with diverticulosis was the same as that of those with irritable colon, namely, a regimen of diet, medication, and hygiene designed to combat spasm, since it has long been the opinion of one of the authors that spasm at the mouth of the diverticulum causes retention of material within the diverticulum with resultant inflammation and infection. During the average follow-up period of 15 years with an undetermined and undoubtedly varying degree of fidelity to the prescribed treatment, complications were noted in 119 of the 294 patients, with the following distribution: diverticulitis in 73 patients (24.8%); hemorrhage in 16 (5.4%); obstruction in 15 (5.1%); and perforation or fistula in 15 (5.1%). Of the 73 patients with diverticulitis, 28 (38%) had superimposed complications, and of the 221 patients with only diverticulosis, 18 (8.1%) had complications without evidence or history of clinical diverticulitis; thus, nearly 5 times as many patients with active diverticulitis had superimposed complications as did those with diverticulosis. Forty patients, i.e., more than half of the 73 with diverticulitis, had only one attack of this complication. Multiple attacks of diverticulitis in the other 33 patients were associated with more than twice as many complications (57.5%) as were single attacks (22.5%). Cancer occurred in 16 (5.4%) of the total group of 294 patients with diverticulosis, with no increase of incidence in areas of diverticulosis or diverticulitis.

These findings have special significance at this time when surgical advances have produced much greater safety in the single-stage resection for diverticulitis and a resultant enthusiasm among many surgeons for earlier radical treatment of this disease. According to the authors, diverticulitis should still be regarded as a medical disease until complications make surgical treatment necessary.

Old and New Tests for Bilirubin in the Urine. J. M. Bleyer and F. Steigmann. Am. J. Digest. Dis. 3:947-952 (Dec.) 1958 [New York].

The investigations described here were undertaken to compare the efficiency and usefulness of 2 older (Rosenbach and Smith) and 2 newer (Franklin and Ictotest) tests for the detection of bile in the urine. Two hundred forty-seven freshly voided morning urine specimens of 129 patients with icteric scleras and clinical and biochemical (liver profile) signs of liver disease were examined for bile and albumin; simultaneously blood was drawn for the determination of the serum bilirubin (van den Bergh). Each urine sample was tested for albumin with 20% sulfosalicylic acid and for bile with each of the following tests: 1. Rosenbach's modification of the Gmelin test: The urine is filtered through a small filter paper. One drop of yellow nitric acid is introduced into the cone of the paper. The appearance of any colored ring indicates positivity. 2. Smith's test: The urine is overlayed with tincture of iodine, diluted with 9 times its volume of alcohol. An emerald green ring at the zone of contact shows the presence of bile pigments. 3. Franklin's bilirubin test: Ten drops of urine are dropped on a tablet made of plaster of paris and containing barium chloride. Two drops of Fouchet's reagent (one-half strength) are added to the surface of the tablets. The presence of bilirubin in the urine is denoted by the appearance of a color ranging from slight bluish-green to deep green. 4. Ictotest: Five drops of urine are placed on an asbestos–cellulose test mat. An Ictotest reagent tablet, containing *p*-nitrobenzenediazonium–*p*-toluenesulfonate, sulfosalicylic acid, sodium bicarbonate, and boric acid, is placed in the center of the moistened area. Two drops of water are dropped on the tablet, allowing the water to run down the sides of the tablet. If the test is positive, the mat around the tablet turns purple.

In addition, 46 urine specimens of 23 control patients with no signs of jaundice and/or liver disease, who had albumin, blood, sugar, or ketone bodies in their urine or had been on different medications, were tested by Ictotest alone to investigate the effect of various urine contents on the Ictotest reaction. Ictotest was found to be the most sensitive. The simple and economical Rosenbach test came close to the sensitivity of Ictotest. The height of the indirect serum bilirubin and the amount of bile in the urine were not always parallel.

SURGERY

Palliative Treatment of Obstructing Processes in the Esophagus and Cardia with Intubation. E. Skielboe. Ugesk. laeger 120:1222-1225 (Sept. 11) 1958 (In Danish) [Copenhagen].

In cancer of the esophagus and cardia, where the possibility of radical operation is excluded and marked difficulty in swallowing even liquid food is not lessened by roentgen-ray treatment, intubation according to Souttar's method seems to be the most satisfactory treatment, except in tumors in the pars superior of the esophagus. In cases in which the tumor is soft or is longer than Souttar's tube, Mousseau-Barbin's plastic tube is useful and requires no special equipment for application. Palliative intubation was carried out in 51 patients with obstructing and mainly malignant processes in the esophagus and cardia—in 41 according to Souttar and in 10 with the Mousseau-Barbin plastic tube. The average time of survival was only 4 or 5 months, but palliative intervention was justified. Souttar's method should be applied generally in preference to gastrostomy, and in suitable cases it is admirably supplemented by Mousseau-Barbin's plastic tube.

Treatment and Prophylaxis of Acute Cardiovascular Insufficiency During Mitral Commissurotomy. S. I. Smelovsky, T. M. Barbinyan and Y. M. Panova. Khirurgiya 34:21-26 (no. 8) 1958 (In Russian) [Moscow].

Acute cardiovascular insufficiency requiring intra-arterial blood transfusion occurred in 46 patients, of a total number of 135, during a mitral commissurotomy performed for stenosis of the left mitral valve. In patients with this complication hypoxia was successfully treated by intra-arterial blood transfusion. Acute cardiovascular insufficiency is caused by the operation itself and by hemorrhage from the left auricular appendage. The weakness of the left ventricle adapted for minimal blood filling also plays a certain role. After dilatation of the mitral orifice this weakness of the left ventricle may give rise to acute insufficiency. Prophylactic intra-arterial blood transfusion is recommended for the prevention of acute cardiovascular insufficiency. Employment of this method, with the administration of epinephrine, during a commissurotomy prevents acute cardiovascular insufficiency. The authors consider that the best site for transfusion is the arteria tibialis posterior. At times the intra-arterial blood transfusion causes pain in the course of the main blood vessels of the lower extremity and paresis of the peroneal nerve. Development of acute cardiovascular insufficiency in 40% of cases of mitral commissurotomy justifies the employment of prophylactic intra-arterial blood transfusion in all cases of surgical treatment of stenosis of the mitral valve.

Mediastinal Chemodectoma. T. J. Madden. Ann. Surg. 148:943-950 (Dec.) 1958 [Philadelphia].

The author reports on a 28-year-old pregnant woman with a mediastinal tumor of aortic body origin which was detected in a routine chest roentgenogram taken in the 6th month of pregnancy. Bronchoscopic examination showed downward displacement of the right upper lobe bronchus. A right-sided thoracotomy was performed, and the entire tumor was removed with a short segment of the innominate artery. Three months later the patient was delivered of a normal female infant. Nineteen months after removal of the tumor the patient was alive and apparently free of disease. Microscopic examination of the operative specimen revealed an extremely vascular tumor, consisting of polyhedral cells with finely granular eosinophilic cytoplasm. The cells were arranged in groups separated by thin fibrous septums. Throughout the tumor there were small clumps of iron-containing, golden-brown pigment. Ten additional cases of carotid-body tumors arising in the mediastinum and in relation to the base of the heart and great vessels were collected from the literature and summarized, together with available recent follow-up data on patients who were living at the time of the original reports.

This summation of experience with mediastinal chemodectomas, together with the known facts about the related and more common tumors of carotid bodies and jugular glomera, is the basis for the following tentative conclusions about the natural history of the tumors. Mediastinal chemodectomas are slow-growing tumors which rarely metastasize but may recur locally after incomplete excision. They occur anywhere in the mediastinum, not necessarily in the usual sites of normal aortic glomera. They may be associated with tumors of similar type in other locations. Surgical treatment may be difficult, and a conservative approach seems to be warranted. Treatment by x-ray is not likely to be effective.

A Report Upon a Patient Five Years Following Resection of the Abdominal Aorta for Recurrent Carcinoma. S. W. Moore. Surg. Gynec. & Obst. 107:709-711 (Dec.) 1958 [Chicago].

The patient was a woman who was 56 years old when she was admitted to the New York Hospital in May, 1952, because of a mass in her abdomen. On Jan. 11, 1949, in another hospital, she had been subjected to an anterior resection of the sigmoid colon for adenocarcinoma with perforation. The abdominal mass detected 3½ years later was firm, fixed, rounded, and 10 cm. in diameter, and lay in the left lower quadrant. At operation on May 21, 1952, a large tumor, 10 by 6 by 4 cm., was found lying between the aorta and the sigmoid colon. Although not fixed, the tumor was adherent to the aorta and to the left common iliac artery. The left ureter entered the mass. There were no metastases in the liver or lymph nodes along the aorta. The tumor was thought to be a local recurrence of the sigmoid carcinoma resected 3½ years previously. To remove the mass, it was necessary to resect en bloc the aorta, both common iliac arteries, and the left ureter together with the tumor. A homograft of abdominal aorta with bifurcation was inserted in the defect by end-to-end anastomosis.

Immediately after operation, there was excellent bilateral pulsation in the femoral and dorsalis pedis arteries. The gross specimens, as well as microscopic sections, showed recurrent carcinoma invading, but not yet penetrating, the lumen of the aorta. Twenty-five days later, on June 16, 1952, the sigmoid colon and left kidney were removed. Four months later, on Nov. 17, a cholecystectomy for chronic cholecystitis with cholelithiasis was carried out without incident. On Oct. 20, 1954, 2 years later, a bilateral subtotal thyroid lobectomy was performed for nontoxic nodular goiter. Now 5½ years have elapsed since resection of the secondary carcinoma, and this patient is quite well save for minor complaints. There is no evidence of cancer, and no loss of weight. Both femoral and dorsalis pedis vessels on both sides are readily palpable with good pulsations.

Prescalene Node Biopsy. K. Cruze, R. F. Hoffman, W. B. Hayden and F. X. Byron. Ann. Surg. 148:895-898 (Dec.) 1958 [Philadelphia].

The authors report on 151 patients, between the ages of 23 and 81 years, on whom 164 prescalene lymph node biopsies were performed with the aid of local anesthesia in the section of thoracic surgery of the Veterans Administration Center in Los Angeles between January, 1953, and October, 1957. A conclusive tissue diagnosis was rendered in 51 (31.1%) of the 164 biopsies. This procedure may prevent needless operation. The indications should include suspected bronchogenic carcinoma or abnormal pulmonary shadows. Bilateral biopsy is indicated in some instances. Prescalene lymph node biopsy yielded positive results in 26 (38.2%) of 68 cases of bronchogenic carcinoma proved by autopsy, clinical, or other ancillary methods. A compilation of the results of prescalene lymph node biopsies reported by other workers and collected from the literature revealed about 30% positive biopsies for all lesions. Complications did not occur when the biopsy was performed with the patient under local anesthesia.

Portacaval Anastomosis: A Study of 12 Pre- and Post-operative Cases. L. Leger and R. Roy-Camille. Presse méd. 66:1673-1676 (Oct. 29) 1958 (In French) [Paris].

Twelve patients with cirrhosis, who had undergone portacaval anastomosis, were followed up for a period of 6 to 18 months after operation. Portal hypertension returned to normal values in 3 patients, it was decreasing over several months in 8 patients, in 2 of whom it began to increase after a while; and it remained unchanged in 1 patient who died of hemorrhage a year after the operation. Another patient died in hepatic coma 21 months after the operation. Clinical improvement, potency of the anastomosis, and cessation of hemorrhage were observed in this series of patients after the surgical treatment. Disappearance of the blood reflux followed the operation, but it returned in a slight degree in 3 patients. Roentgenologic examination of esophageal varices in 7 patients after the operation showed that they remained unchanged in 1 patient and diminished in 6. Liver function improved in 1 patient, remained unchanged in 2, and deteriorated in 4.

Contributions to Surgical Treatment of Portal Hypertension. M. A. Khelimsky. Khirurgiya 34:10-14 (no. 8) 1958 (In Russian) [Moscow].

Splenectomy with simultaneous omentohepatofixation and omentorenopexis was employed by the author in patients with the syndrome of portal hypertension and with thrombophlebitic splenomegaly and splenogenic cirrhosis of the liver. He operated on 11 patients who were admitted to the clinic because of hemorrhages due to varicose veins of the esophagus. There were 6 men, 4 women, and a 13-year-old girl. After the operation a normal blood picture was reestablished in all the patients, and thrombopenia, ascites, and hemorrhages disappeared. Ten patients have resumed their work. One patient in whom omentohepatofixation alone was performed without omentorenopexis died 1½ years after the operation as a result of thrombosis of a branch of the superior mesenteric artery.

Emergency Surgery for Severe Upper Gastrointestinal Hemorrhage: An Analysis of Sixty-Four Cases. W. E. Switzer and W. W. Nichol. A. M. A. Arch. Surg. 77:843-850 (Dec.) 1958 [Chicago].

This report is concerned with patients who were operated on as emergencies because of severe upper gastrointestinal bleeding. The case series was accumulated during the years from 1950 through 1957 at a large Army hospital and includes active-duty military personnel and their dependents, retired military personnel, and Veterans Administration beneficiaries. Not included are the many patients whose bleeding ceased with conservative treatment or those persons who were operated on electively after a bleeding episode. During the period mentioned, 353 patients entered the hospital with upper gastrointestinal bleeding. Sixty-four (18.1%) were operated on. All but 2 of these 64 patients were men. The ages of the patients ranged from 17 to 74 years; 33 were under, and 31 were over, 50 years of age. There was an increase in the number of patients requiring surgery for gastrointestinal bleeding in the fall. The month of November alone accounted for 12 (18.8%) of the entire group, in contrast to July when no operations were done for gastrointestinal bleeding during the entire 8-year period. Both hematemesis and melena occurred in 44 patients, melena only in 13, and hematemesis only in 7.

After commenting on preoperative hemoglobin and hematocrit values, on transfusion requirements, preoperative endoscopy, and roentgenoscopy, the authors state that 56 of the 64 patients were treated by subtotal gastric resection, and 2 by total resection. The remaining 6 patients were treated by one of the following: ligation of the bleeding gastric ulcer; suture of a stomal ulcer; exploration and pyloroplasty; suture and packing of ulcer; exploration only; and suture of laceration at the gastric cardia associated with repeated vomiting (Mallory-Weiss syndrome). The following points are emphasized: 1. These patients benefited from a combined medical-surgical evaluation of their problem. 2. The results of the early diagnostic procedures of endoscopy and upper gastrointestinal x-rays appeared to justify the effort required, without undue risk to the patients. 3. Blood transfusion requirements in these patients should be thought of in terms of one-half to several times the patient's estimated normal blood volume. 4. Although the mortality rate in the above-50 age group was more than triple that of the below-50 age group, it was also true that the lives of 24 of the 31 patients above 50 years were prolonged by surgical intervention. 5. Recurrent bleeding and sepsis were the complications most frequently associated with death.

Favorable Postgastrectomy Results in Billroth II Patients with a Small Stoma. J. J. McCaughan Jr. and R. F. Bowers. A. M. A. Arch. Surg. 77:837-842 (Dec.) 1958 [Chicago].

The Billroth 2 type of gastric resection has been widely accepted, because it has the lowest peptic ulcer recurrence rate of any of the procedures in use, while the mortality and immediate morbidity rates are comparable. However, the late postgastrectomy findings of weight loss, diarrhea, and the dumping syndrome with accompanying weakness are believed to be more frequent than with other procedures, notably gastroenterostomy and the Billroth 1 procedure. The postoperative study of patients who have undergone the Billroth 2 type of gastric resection suggests that the symptoms are due to loss of the pyloric sphincter and stomach, which is usually associated with rapid emptying of the stomach. This sudden flow of food and fluid into the jejunum must be slowed down. To test the validity of this concept, the authors deliberately formed a small stoma in the Billroth 2 operation. The purpose of the small stoma was to retard the gastric emptying. Roughly, 1.5 to 2.5 cm. has been the selected size of the small stoma, although this cannot be accurately measured. A stoma of 2.5 to 6 cm., or larger, is regarded as large by the authors. They found some large stomas of the Pólya type to be from 4 to 6 cm. in diameter. The measurement of the stomas is not accurate, but is estimated by the surgeon with finger and thumb.

The authors compared the results obtained by Billroth 2 gastrectomy in 100 patients with small stomas with those in 100 with large stomas. Follow-up studies by personal interview revealed that the postgastrectomy syndrome was reduced approximately by one-half in the small-stoma group as compared with the control group. Weight loss was reduced from an average of 9.83 lb. in the control group to 3.84 lb. in the small-stoma group. Weakness, which seemed to be the commonest and severest complaint of the control group, was decidedly better in the small-stoma group. Diarrhea was approximately equal in frequency in the two groups. Subtle distinction in postcibal symptomatology in the two groups did not seem feasible in this series. If there was doubt about the presence of postgastrectomy symptoms, the authors used the oral glucose intake test (250 cc. of 50% glucose by mouth), which proved to be very practical and produced the symptoms if the patient had really experienced the postgastrectomy syndrome. It was often difficult to separate psychosomatic symptoms from the actual ones, but the glucose test was helpful in these instances. A small number of patients experienced the dumping syndrome even when stomal obstruction was present.

Making the partially obstructing stoma proved difficult. At the end of the operation, the surgeon often could not predict the degree of stomal obstruction that would follow. The best results were obtained from stomas that would just admit one small finger.

Gastric Polyps. K. Kettunen. Ann. chir. et gynaec. Fenniae 47:300-312 (no. 4) 1958 (In English) [Helsinki].

Of 14,566 patients who underwent roentgenologic examinations in the department of roentgenology of the Maria Hospital in Helsinki between 1948 and 1955, gastric polyps were detected in 37. The author reports on these 37 patients (15 men and 22 women), whose ages ranged from 32 to 88 years, with an average age of 60.2 years. Epigastric distress and pain were the most prominent and significant complaints. Achlorhydria was found in 19 of 21 patients tested. Four patients had pernicious anemia. Malignant transformation was present in 3. Thirteen of the 37 patients had single gastric polyps, 4 had 2 polyps, and 20 had 3 or more. Generalized polyposis was present in 3 patients.

Treatment in 26 of the 37 patients was conservative, while partial gastric resection was performed on 7, exploratory operation on 1, simple excision on 2, and subtotal gastric resection on 1. It is suggested that roentgenologic examinations, with the aid of barium as contrast medium, be used in establishing a diagnosis of gastric polyps; gastroscopic examination should be used as a supplement to the roentgenographic study, since it may reveal polyps overlooked by the latter method and vice versa. If malignant disease cannot be determined on the basis of gastroscopic or roentgenologic examination, an exploratory operation is recommended.

Excisional Treatment of Aneurysm of Celiac Artery. H. B. Shumacker Jr. and H. Siderys. Ann. Surg. 148:885-889 (Dec.) 1958 [Philadelphia].

Of 35 patients with aneurysm of the celiac artery, whose cases have been reported in the literature, 31 died of rupture. None of the patients was treated successfully by surgery. This fact prompted the authors to present the case of a patient with multiple arteriosclerotic abdominal aneurysms, who has recently been treated successfully by surgery. The patient was a 41-year-old woman who was admitted to the department of surgery of the Indiana University Medical Center in Indianapolis in August, 1957. Aneurysms of the celiac axis, the splenic artery, and both common iliac arteries were excised. Ischemia of the stomach and liver followed temporary occlusion of the celiac artery and was obviated after resection of the celiac aneurysm by anastomosis of the remaining stump of the celiac artery and the main hepatic artery. Aortic-iliac continuity was restored by insertion of a bifurcation graft. The patient had an uneventful convalescence and was discharged on the 12th postoperative day. In view of the extent of her arteriosclerotic disease and the high normal level of her serum cholesterol, she was placed on a low-cholesterol and low-fat diet. When she was seen 3 months later, she was well and had been working full time. The liver edge was not palpable, and the peripheral pulses were excellent.

Congenital Pyloric Stenosis Treated by the Ramstedt Operation: A Review of 1,018 Cases. S. Feggetter. J. Internat. Coll. Surgeons 30:696-700 (Dec.) 1958 [Chicago].

The author reports on 1,018 children with congenital pyloric stenosis, who underwent the Ramstedt operation in Newcastle, England, between 1940 and 1956. Seventeen children died, representing a mortality rate of 1.6%. The operative and postoperative complications are listed, and a typical case in a 4-week-old boy is described. Medical accounts refer occasionally to congenital pyloric stenosis from the year 1700 onward, but the first accurate description of the disease was presented by Hirschsprung in 1887. All the signs and symptoms result from obstruction due to a pyloric tumor, which is caused by true hypertrophy of the circular muscle of the pyloric canal. The development of the tumor depends on the presence of a recessive gene; it is to be expected, therefore, that the incidence of the anomaly will increase. It now occurs in approximately 3 of each 1,000 live births. In 1946, the over-all mortality rate in England and

Wales was 20%. The differential diagnosis includes infectious vomiting, pylorospasm, and the intestinal atresias. The treatment of choice is the Ramstedt operation performed with the aid of open ether anesthesia. It has been observed that, when children in a given area have been treated by one or two surgeons interested in this type of work, with the assistance of a pediatric team and a skilled anesthetist, the results of the Ramstedt operation have been substantially improved.

Surgical Treatment of Disease of the Prostate in Patients with Diabetes Mellitus. H. Eufinger and D. Borm. Beitr. klin. Chir. 197:11-15 (no. 1) 1958 (In German) [Munich].

The authors report on 12 men, between 56 and 81 years, with disease of the prostate and diabetes mellitus who were operated on at the surgical clinic of the University of Kiel, Germany, between 1947 and 1956. Of the 12 patients, 9 had adenoma of the prostate, and 3 had carcinoma of the prostate. Ten patients underwent electroresection, and 2 were subjected to suprapubic prostatectomy according to Freyer. Four of the 10 patients required a second resection, and, therefore, 16 operations were performed on the 12 patients. The blood sugar values of the patients varied between 122 and 257 mg. per 100 cc., and the amounts of sugar excreted in the urine varied between 0.59 and 14.7 Gm. The diabetes mellitus was discovered in 3 patients only after admission to the surgical clinic, and its duration in 4 patients varied between 17 and 23 years. Six patients were hospitalized because of acute retention of urine, with 300 to 2,000 cc. of fluid contents of the bladder, and the other 6 were hospitalized because of dysuria and pollakiuria. One of the patients died on the third postoperative day of pulmonary embolism. The remaining 11 patients were discharged from the hospital, and 10 were followed up after their discharge. One died 8 days later at home, one who had carcinoma of the prostate died 4 years after the operation, and one died 2 years after the operation. The remaining 7 patients are still alive and free of complaints of micturition. Four patients no longer require treatment with insulin. In 3 of these, the disease of the prostate caused a latent diabetes mellitus in patients of advanced age to become manifest, but the diabetes became latent again after surgical treatment of the prostate. Three patients are still receiving insulin, but the diabetic disturbance of metabolism is controlled by the drug.

These findings show that diabetes mellitus does not represent a contraindication to surgical intervention in patients with disease of the prostate. It seems that the type of the surgical procedure and the preoperative and postoperative administration of antibiotics and chemotherapeutic preparations, respectively, are of far less importance in the surgical treatment of diabetic patients with disease of the prostate than the preoperative control of the diabetic metabolism by the internist.

Importance of Early Operation in Congenital Atresia of the Extrahepatic Bile Ducts: Report of 10 Proved Cases. G. E. Schnug. Ann. Surg. 148:931-936 (Dec.) 1958 [Philadelphia].

The author reports on 10 newborn infants with obstructive jaundice caused by congenital atresia of the extrahepatic bile ducts. Five of these had atresia of the extrahepatic bile ducts which was surgically correctable. Two of the 5 were operated on, one successfully, at the age of 2 months, and the other unsuccessfully at the age of 6 months; the other 3 patients were not operated on, but autopsy revealed that the anomalies had been correctable. Marked liver changes secondary to atresia of the bile ducts were observed on autopsy. Even the one infant who was operated on successfully had advanced cirrhosis of the liver. She survived several hemorrhages and reached the age of 3 years, at which time it was felt that her vessels were large enough so that a splenorenal shunt could be made. Splenectomy also was done, and the patient is now a normal 5½-year-old girl. Her liver function has gradually improved over a period of years. In the 291 patients with congenital atresia of the extrahepatic bile ducts, whose cases were collected from the literature, the cause of death was most frequently failure of the liver. The atresia was surgically correctable in 68, and only 24 of these were reported as cured. It was also noted that almost all successfully treated patients were operated on when they were less than 2 months old.

Available diagnostic measures are inadequate in differentiating the various types of obstructive jaundice in the newborn infant. The reported data show that irreversible changes in the liver do occur early in patients with biliary atresia. Exploration within the first months of age has been recommended. Anastomosis between the extrahepatic biliary tree and the duodenum is the simplest and probably the procedure of choice. It seems quite definite that the liver damage and the complications and sequelae resulting from the damage are the cause of the poor results in the treatment of patients with correctable biliary atresia.

Antibiotic Therapy: Adverse Effects in Acute Appendicitis Before Diagnosis. R. B. Dietrick, C. W. Byrd and J. A. Lawson. Ann. Surg. 148:985-990 (Dec.) 1958 [Philadelphia].

Of 46 patients with acute appendicitis who were admitted to the surgical service of the Veterans Administration Hospital in Richmond, Va., between 1955 and 1957, 5 (10.9%) had been treated with antibiotics or sulfonamides before a diagnosis was established or before an operation was performed.

The authors believe that this therapy obscured the symptoms of appendicitis and thereby delayed and made the diagnosis more difficult. As a result of being unable to reach an early diagnosis, the morbidity, length of hospital stay, and expense of hospitalization were greatly increased. The experience with these patients indicates that appendicitis treated with antibiotics may lead to 2 different clinical pictures: (*a*) patients who are obviously ill, who have masked and atypical symptoms, and who require exploration on the basis of the clinical picture and (*b*) patients whose symptoms are so completely masked that no specific diagnosis can be made, who do not appear to require exploration on the basis of their clinical findings, and who settle into a state of chronic disability which may extend over many months, with occasional exacerbations.

The 5 patients treated with antibiotics had a large number of complications, either directly or indirectly, due to their primary disease. In one patient a severe wound infection developed, and he also required a skin graft to an ulcer caused by extravasation of arterenol, which was given to correct persistent severe hypotension postoperatively; an abscess arose in his McBurney scar 18 months after operation. Intestinal obstruction was caused in another patient by a volvulus about the point of adherence of the inflamed appendix to the terminal ileum. In a third patient persistent rectal stenosis occurred at the site of adherence of the appendix to the rectum. In still another patient gross hematuria was caused by genitourinary manipulations, and intestinal obstruction due to a great number of postoperative adhesions, resulting from chronic inflammation over a period of many months, required reoperation. Patients with undiagnosed abdominal pain should not receive antibiotics until appendicitis can definitely be excluded as a diagnosis. In patients admitted with abdominal pain in whom the symptoms are atypical, the examining physician should have a high index of suspicion that the patient may have received antibiotic therapy and should closely question the patient concerning this possibility. When the patient gives such a history, early exploration is indicated despite the paucity of physical findings.

Differential Diagnosis of Mitral Pathology. B. V. Petrovski and V. V. Zaretski. Vestnik khir. 81:28-33 (Nov.) 1958 (In Russian) [Leningrad].

Electrokymography (study of pulsations of various segments of the peripheral contour of the heart) has been successfully applied in the diagnosis of heart anomalies, 128 commissurotomies having confirmed its findings. The left atrium electrokymogram reveals best of all the peculiarities of mitral defects. The left atrioventricular valve stenosis is reflected by an inhibited and prolonged systole of the left atrium, the electrokymogram showing a diastolic plateau. After the atrial systole is over, a mitral valve insufficiency is disclosed by a regurgitation reflux indentation on the electrokymogram of the left atrium during the systole of the left ventricle. The existence of mixed mitral defects is evidenced on the electrokymogram by elements of left venous orifice stenosis and mitral valve insufficiency, the more advanced anomaly being revealed by the prevalence of its characteristics.

Clinical and Functional Assessment of Surgical Treatment of Mitral Stenosis: A Follow-Up. A. L. Izbinski and T. G. Blestkina. Vestnik khir. 81:33-40 (Nov.) 1958 (In Russian) [Leningrad].

Treatment of 110 patients by mitral commissurotomy is evaluated in a follow-up ranging from 6 months to 4 years. A favorable outcome was found in 86% of the cases. An adjuvant classification of third-degree competence of the "second barrier," devised by Izbinski and his co-workers, was added to the usual classification of blood circulation impairment in the preoperative and the postoperative assessment of the patient's condition. By "second barrier" the authors refer to the complex of pathological changes in the pulmonary parenchyma and in the pulmonary circulation developing on the basis of mitral stenosis. The unfavorable results were found to depend on (1) a failure of the commissurotomy itself, (2) a rather late recrudescence of rheumatic infection, (3) marked dystrophic myocardial changes, (4) intercurrent diseases, and (5) clear-cut symptoms of the "second barrier" complex before the operation. This adjuvant classification gives a more reliable appraisal of the patient's condition before surgery and has an important significance for the prognosis of late results. A fourth-degree circulatory impairment does not preclude surgical treatment of mitral stenosis, because an effective commissurotomy is often followed by a marked improvement in the patient's condition and even by a partial return to work fitness.

Indications and Contraindications for Shunt Operations in Portal Hypertension. S. Brandstaetter. Harefuah 55:242-243 (Nov. 16) 1958 (In Hebrew with English Summary) [Tel-Aviv, Israel].

According to Brandstaetter, a brief survey of the newer techniques indicates that splenoportography and measurement of the splenic pressure are the best methods available for determining whether portal hypertension is the cause of esophageal varices in a given case and whether portal hypertension is due to intrahepatic or extrahepatic block. In a patient with bleeding varices and portal hypertension, intrahepatic block is a clear indication for a shunt operation. Laboratory tests suggested by Linton proved to be a relatively reliable index in the selection of patients for portacaval shunt. A patient with repeated hemorrhages and borderline liver function tests is a bad risk for splenorenal shunt, and portacaval shunt is contraindicated. Uncontrollable ascites remains a contraindication to shunt procedures until more reliable statistical material has been gathered. As even in good-risk patients the operative mortality is still about 10%, the advisability of prophylactic shunt in patients with cirrhosis and varices who have never bled is still a moot problem.

The Use of Controlled Hypothermia for the Prevention of Ischemic Renal Damage Produced by Cross-Clamping of the Thoracic Aorta: Experimental Observations. R. Benvenuto and M. Serratto. Minerva med. 49:3948-3952 (Oct. 20) 1958 (In Italian) [Turin, Italy].

A study on hypothermia induced to protect the kidney against ischemic damage due to occlusion of the thoracic aorta is reported. The experiment was carried out on 18 male and female dogs, each having a body weight of 15 to 20 kg., divided into 2 groups. The first group was composed of 12 animals, 6 used as controls and operated on at a normal temperature and 6 operated on under hypothermia; a series of biopsies of the kidney was carried out in these animals after the operation. The second group was composed of 6 animals, 2 used as controls and operated on at a normal temperature and 4 operated on under hypothermia. Anesthesia was induced in all dogs with intravenous injections of Nembutal, 30 mg. per kilogram of body weight, and respiration was controlled by means of tracheal intubation and of a mechanical respirator. In the dogs subjected to hypothermia, the temperature was reduced to 32 C (89.6 F) by means of thermal blankets at the moment that the thorax was being opened, and to 28 C (82.4 F) when occlusion of the aorta by cross-clamping took place. Normal temperature, 37 C (98.6 F), was restored by introducing hot water in the thermal blankets. Occlusion of the aorta for one hour caused necrosis of the convoluted tubules of the kidney in all the animals used as controls. Biopsy performed soon after the restoration of normal temperature, and 24 and 36 hours after the operation, revealed no necrosis of kidney tissues in the animals operated on under hypothermia.

Necrosis of the proximal tubule, already on the way to recovery, was noticed in one animal on which biopsy was performed one week after the intervention. This animal also presented signs of spontaneous nephritis. Kidney function was seriously impaired in all the control dogs soon after the operation; it improved later, but it never returned to the condition it was before operation. In the dogs operated on under hypothermia, kidney function was slightly but temporarily impaired. Normal values were obtained in clearances carried out 1 or 5 weeks after the operation.

Rheumatoid Tenosynovitis: Diagnosis and Treatment. T. A. Potter and J. G. Kuhns. J. Bone & Joint Surg. 40A:1230-1235 (Dec.) 1958 [Boston].

The authors report on 154 patients with rheumatoid tenosynovitis who were treated at the Robert Breck Brigham Hospital in Boston and were followed for periods exceeding one year. Of these, 65 with only small swellings were treated conservatively with heat and support. Thirty of these have been cured, i. e., the tenosynovitis has disappeared and has not recurred. In 10, the lesion has become smaller but is still present; the remaining 25 did not respond to this method of treatment. Thirty-five patients with circumscribed lesions not larger than 1 in. in diameter were treated by injection of hydrocortisone, repeated at 2-week intervals; 15 of these showed complete disappearance of the swelling, the condition of 5 was improved, and 15 were therapeutic failures. In 30 patients with masses on the tendons larger than 1 in., the lesions were excised; 20 patients were relieved completely and had no recurrence, 3 had a slight recurrence of the swelling, and 7 had an early recurrence of the lesion. Tendon repairs, including resuturing, grafting, and transferring of tendons, were performed on 24 patients; in 10 of these the operation restored good function, improvement in function was observed in 2, and 12 were therapeutic failures.

Rheumatoid tenosynovitis is a common complication of rheumatoid arthritis; its slow, nonpainful development often results in failure of recognition and diagnosis. This lesion is found most commonly on the dorsum of the wrist, involving the extensor tendons. Diagnosis can be established only by microscopic examination of the diseased tissue. It can be suspected when swelling appears in and upon the tendons in the presence of rheumatoid arthritis. Treatment in the early stage should include heat, support, and relaxation of the tendon. It may be supplemented by injections of hydrocortisone into the mass every 2 weeks. When the swelling becomes large, excision of the diseased tissue as completely as possible is advised. Rupture of tendons requires surgical repair. No relationship could be established between rheumatoid tenosynovitis and Quervain's disease and snapping finger.

The Value of Shunt Operations for Portal Hypertension. D. Erlik. Harefuah 55:233-238 (Nov. 16) 1958 (In Hebrew with English Summary) [Tel-Aviv, Israel].

Of 17 shunt operations for portal hypertension, 10 were splenorenal shunts and 7 were portacaval shunts. Two of these shunt operations performed for Budd-Chiari syndrome were not analyzed. Shunting was performed for cirrhosis of the liver in 13 patients, and for extrahepatic block in the remaining 2. Of 6 patients on whom portacaval shunt was performed, 2 died within 10 days of the operation, but in these the liver function tests indicated that death was caused by hepatic insufficiency leading to coma. The other 4 patients are in satisfactory condition from 1 to 3 years after the operation; the severe preoperative hemorrhages did not recur. No deaths attributable to the operation occurred in 9 patients undergoing splenorenal shunts, but 3 of these patients died because of recurrent esophageal bleeding 2 weeks, 6 months, and 2 years, respectively, after the operation. The shunt was found to be thrombosed in all fatal cases. The progress of the other 6 patients was satisfactory with no recurrence of bleeding.

On the basis of these observations and of literature reports, the author concludes that shunt operations are serious procedures owing to the dangers of immediate and delayed complications. The decision to perform a shunt operation requires thorough study of the individual patient, but there should be no wavering if operation is required. In case of severe hemorrhage from esophageal varices, a shunt should be performed before another bout of bleeding may be fatal.

The choice of shunt is a source of controversy. The portacaval shunt is the best as regards function and, therefore, the most reliable in preventing hemorrhage, but for this type liver function tests must at least be fair. When the liver tests are seriously impaired, the splenorenal shunt is preferable, although it is prone to closure by thrombosis. This type of shunt gives excellent results in extrahepatic block. Shunt operations should not be performed to prevent anticipated hemorrhage. The only exceptions are cases in which splenectomy is performed for congestive splenomegaly with severe hypersplenic phenomena. In these cases the splenic vein should be saved from thrombosis by performing a "prophylactic" splenorenal shunt. When severe and repeated hemorrhages from esophageal varices occur at short intervals, a Blakemore tube should be introduced into the esophagus to stop the bleeding. Then a suitable shunt is constructed with the balloon still in place. One or 2 days after the operation the balloon can be removed without danger of further bleeding.

Antibiotics for Colon Surgery. I. Cohn Jr. Gastroenterology 35:583-591 (Dec.) 1958 [Baltimore].

Evaluation by standardized methods of 28 agents for intestinal antisepsis permitted their division into recommended and less satisfactory groups. All the groups recommended for general use in intestinal antisepsis are combinations of neomycin with another poorly absorbed agent. A clinical trial of a triphasic antibiotic administration program was undertaken in patients who were subjected to surgical intervention on the colon; these patients were selected from the Louisiana State University surgical service at Charity Hospital of Louisiana and from 4 other hospitals in New Orleans. The 3 phases of the program were as follows: (1) preoperative preparation with a combination of 1 Gm. of neomycin and 200 mg. of tetracycline (Achromycin) given every hour for 4 hours, then every 6 hours for a total of 72 hours; (2) intracolonic instillation of a powder containing 250 mg. of tetracycline and 1.25 Gm. of neomycin into the lumen of the colon whenever the colon was opened for any reason; and (3) postoperative intraluminal injection of a mixture of 150 mg. of tetracycline and 750 mg. of neomycin, dissolved in 10 cc. of sterile saline solution; this mixture was injected 3 times daily for the first 5 postoperative days through a plastic tube, which was inserted into the colon proximal to the point of anastomosis of colotomy and exteriorized through a stab wound.

Between July 1, 1955, and Dec. 31, 1957, 200 patients were evaluated on this antibiotic program for colon surgery. No cases of pseudomembranous enterocolitis were observed, and the absence of fistulas and of peritonitis in the 67 patients who received postoperative treatment through the plastic tube encouraged further study of this form of therapy. Complications were not completely eliminated in these surgical patients, though, and it should not be expected that any amount of antibiotic therapy would eliminate all complications, nor should such therapy replace sound surgical principles. Clinical experience with these 200 patients over 2½ years has substantiated the experimental evidence that a high concentration of antibiotics should be maintained within the lumen of the intestine before, at the time of, and after surgical intervention on the colon.

Arthrogryposis Multiplex Congenita. N. G. Mead, W. C. Lithgow and H. J. Sweeney. J. Bone & Joint Surg. 40A:1285-1309 (Dec.) 1958 [Boston].

During a period of 31 years, 68 patients with arthrogryposis multiplex congenita were treated at the Shriners' Hospital for Crippled Children in Chicago. The authors report on 40 of these, who were examined and treated and on whom close follow-up studies were carried out. Twelve patients were followed from infancy into adulthood. All 4 extremities were involved in 20 patients, both lower extremities in 11, both lower and one upper extremity in 7, both upper extremities in 1, and one lower and one upper extremity in 1. The causation and pathology of arthrogryposis are not well understood, and there is no general agreement concerning them. Until the true nature of this congenital disorder, which is characterized by multiple rigid joint deformities, is known, there is little advantage in using other terms for the condition. The occurrence of the disease in one member of each of 4 sets of identical twins, 2 of which are in this series, seems to exclude hereditary factors as the cause and to cast doubt on theories of intrauterine mechanical, circulatory, or toxic causes. The negative family histories further tend to exclude the theory that heredity is a cause.

The primary pathological site may be either in the spinal cord or in the muscles. It is believed that the fibrosis around the joints and in the subcutaneous tissues is a part of the pathological process and not merely secondary to intrauterine inactivity. Mental deficiency is infrequent in patients with arthrogryposis. When present, it does not appear to be more than coincidental. Only 2 of the 40 patients were considered to be below normal in intelligence; one of these had cerebral palsy also, and it was felt that the mental deficiency was related to this condition. The joint deformities are difficult to correct and to maintain in correction. Function may be poor because of stiffness or lack of muscle power even when the deformity has been overcome. Stiff joints must be placed in the position of function, and unstable limbs must be braced for weight bearing. If these things are accomplished, results will be satisfactory. Patients with arthrogryposis, even though severely handicapped, generally make a satisfactory adjustment and live successful lives. Severe pain is not often present despite the poor mechanics many of these people must endure.

Congenital Pseudarthrosis of the Tibia. H. B. Boyd and F. P. Sage. J. Bone & Joint Surg. 40A:1245-1270 (Dec.) 1958 [Boston].

The authors report on 9 girls and 6 boys with congenital pseudarthrosis, who were operated on at the Campbell Clinic-Hospital in Memphis, Tenn. Of the 15 patients, 7 who were treated between 1941 and 1948 have reached skeletal maturity, and end-results are reported not only regarding treatment but also regarding social and economic status. The remaining 8 were operated on after 1948, and since none of these have reached skeletal maturity, they cannot be included in an end-result study. All 7 patients in the first group had repeated reconstructive operations: 1 of these was a surgical failure because treatment resulted in below-the-knee amputation; 3 had moderate results, 2 of them requiring braces and 1 requiring a shoe elevation; 3 were operated on successfully, having no longer complaints referable to the lower extremities. From a social and economic point of view treatment was successful in 6 of the 7 patients. The one surgical failure was a social and economic success.

There are two distinct types of congenital pseudarthrosis of the tibia. In the first, a cystic defect, with or without fracture, is present, and the pathological findings resemble those in fibrous dysplasia. The second shows sclerosis and tapering of the bone ends, probably due to a constricting band of fibrous tissue. In this type, union is more difficult to secure. The causative factors are still undetermined, but congenital pseudarthrosis is probably due to a maldevelopment of the mesodermal structure during the 5th week of fetal life, with an associated abnormality occurring in the nerve pathways to the affected leg. Early surgical treatment before the development of marked deformity is advised. In the first type, the cyst should be curetted and the defect filled with bone chips; additional bone grafting may or may not be necessary. In the second type, a wide resection of the constricting band of pathological soft tissue should be done, combined with suitable bone grafting and adequate internal and external fixation; the latter, achieved by casts followed by suitable braces, should be continued until skeletal maturity or until a tibia of relatively normal size develops. In patients with extreme deformity, amputation may be indicated when one is reasonably sure that a prosthesis will provide a better weight-bearing extremity than the best extremity that could be obtained after successful reconstructive surgery. In making the decision, the surgeon should compare the function of an artificial leg with the best result that can reasonably be expected after reconstructive surgery, not with a normal extremity. Repeated clinical and roentgenologic examinations should be continued until skeletal maturity is reached. If at any time evidence of narrowing of the bone or sclerosis of the medullary cavity appears, prophylactic operative intervention with wide resection of the constricting band of scar tissue should be done. In addition, reinforcing grafts should be placed about the area of previous pseudarthrosis. Multiple operations may be necessary during the growth period. A registry for congenital pseudarthrosis of the tibia is needed in order to enhance knowledge of the causation, pathology, treatment, and end-results through the age of skeletal maturity.

Significance of Mineral Metabolism in Surgery. E. Carstensen. Chirurg 29:536-541 (Dec.) 1958 (In German) [Berlin].

The author studied the metabolism of water and minerals in 80 patients who underwent operations of moderate or extensive type at the surgical clinic of the University of Hamburg–Eppendorf, Germany; these included such surgical interventions as gastrectomy, cholecystectomy, amputation of the rectum, pulmonary resection, strumectomy, and radical removal of mammary glands. The studies of metabolism were carried out preoperatively and postoperatively. In the course of and after the surgical intervention, the patients were given infusions of dextrose and fructose without the addition of minerals. Rarely the amount of transfused citrated blood exceeded 250 to 500 cc. The variations in electrolytes in the serum and the urine were markedly uniform, independently of the extensiveness of the surgical intervention, provided that no complications occurred in the field of the operation. After increased elimination of potassium on the first and the second postoperative day, the potassium reached its lowest value in the serum on the 3rd or the 4th postoperative day. On the 6th or the 7th postoperative day, the serum potassium level and the potassium elimination became normal again. It seems likely that the increased postoperative potassium elimination by the kidneys and the resultant relative hypopotassemia may be a sequela of the stimulation of the adrenal cortex by the "operative stress." Postoperative determination of the cortisone serum level revealed that it was considerably increased and that the highest value was reached 6 hours after the operation. On the 5th postoperative day the cortisone serum level was restored to normal. The postoperative hypopotassemia seldom reached values of less than 4 mEq. in the serum. The term "compensated hypopotassemia" is suggested because of the absence of clinical symptoms and since the condition does not require any therapeutic measures.

Decompensation of the electrolyte and particularly of the potassium metabolism threatens only after postoperative complications, such as peritonitis, ileus, major suppuration, and intestinal fistulas. Prolonged postoperative feeling of thirst for more than 2 or 3 days, or increasing thirst, is suggestive of the onset of such complications. Increased loss of potassium may be manifested by feeling of weakness, hypotonia of the skeletal muscles, cyanosis of pulmonary origin, atonia of smooth muscles, nausea, and vomiting. The organism then is no longer able to compensate spontaneously for the potassium loss, and administration of infusion solutions containing electrolytes and carbohydrates becomes indispensable. The electrolyte losses of patients with an uneventful postoperative course are clinically insignificant, and electrolyte substitution therapy is not necessary. An exaggerated infusion activity may even be more harmful than useful. Therapeutic electrolyte infusions with flame-photometric control are required in patients with postoperative complications occurring in the operative field.

Potassium Metabolism and Potassium Substitution Therapy in Patients Subjected to Surgical Interventions. G. M. Dummer. Chirurg 29:541-544 (Dec.) 1958 (In German) [Berlin].

In the course of surgical intervention and in the postoperative phase, potassium exerts a particular influence on the biological behavior, i. e., on the composition and distribution of electrolyte solutions in the 3 body spaces of the patient, namely, the cell, the interstice, and the intravascular space. Every normal operative intervention is associated with a loss of potassium. Intracellular acidosis with alkalosis of the extracellular fluid results from a change in hydrogen ions. In the absence of postoperative complications the organism is able to compensate for the alkalosis of the extracellular fluid, but the acidosis in the cells may be compensated for only when the organism has taken up again adequate amounts of potassium and monosaccharides and a normal glycogenesis has been reestablished.

The symptoms of potassium deficiency, i. e., a serum potassium level of less than 13 mg. per 100 cc. (3.3 mEq. per liter), may vary from general weakness to flaccid paralysis of the extremities with abolition of tendon reflexes; they have often prevented an operation from being successful. The request, therefore, is advanced to provide for potassium substitution before, in the course of, and after the surgical intervention. Substitution by mouth represents the most favorable method. Fruits, vegetables, meat, milk, and their derivatives are rich in potassium, but it is difficult to compute a diet with an excess in potassium while commercial potassium salts can be added easily to the diet. Oral administration of potassium, however, is rarely feasible in surgical patients, and, therefore, infusion treatment is the method of choice.

Two groups of surgical patients must be distinguished as follows. The first group consists of those without significant preoperative or postoperative potassium loss, and the second group consists of those with a preoperative potassium deficiency or those in whom a major postoperative loss of potassium is caused by the necessary removal of gastric juice and intestinal juice respectively. The solution used for patients in the first group should contain 2 Gm. of potassium chloride per liter, corresponding to about 1 Gm. of potassium. It should also contain sodium chloride. Up to 1,500 cc. of such a solution was used by the author with highly satisfactory results on the day of the operation, and amounts of 500 to 1,000 cc. were given on the following days according to need. The pH value of 7.2 of this solution corresponded with the blood pH. The addition to the solution of 25 Gm. of dextrose and 25 Gm. of fructose accelerated the transport of potassium into the cell body. In patients with severe hypopotassemia, an adequate amount of sterile 10% potassium chloride solution and dextrose was added to the infusion solution. The use of a flame photometer for serum potassium and sodium determinations is strongly advocated.

NEUROLOGY & PSYCHIATRY

Leucotomy for Pain. A. Elithorn, E. Glithero and E. Slater. J. Neurol. Neurosurg. & Psychiat. 21:249-261 (Nov.) 1958 [London].

The authors report on 13 men and 12 women, between the ages of 31 and 78 years, who underwent operations of leukotomy type for the relief of intractable pain and were followed up for periods ranging from 17 to 78 months, with an average of 40 months. Nine patients had "extensive" operations, consisting of full bilateral "standard" operation in 7 and full unilateral operation with partial incision on the contralateral side in 2. Three patients had only a unilateral standard leukotomy, and 13 patients had "limited" operations in which half or less of the white matter of the frontal lobes was divided. The results of the operations were assessed by the patient and by the relative most concerned, clinically; they also were assessed with a rating scale, including symptoms, employment, family relationships, and community relationships, thus still depending on the subjective evaluation of quantitative data but, nevertheless, permitting a more detailed assessment of the efficacy of the treatment.

Clinical evaluation suggested that 17 of the 25 patients had been clearly helped by the operation. Twenty (80%) showed an over-all gain on the social rating. However, only 8 (35%) of 23 patients and 8 (38%) of 21 relatives thought that the operation had been worthwhile. The tendency for patients and relatives to be dissatisfied with a leukotomy for intractable pain was related to the observation that, although most patients admitted to some improvement in their symptoms, only 5 thought that their pains were less intense. With regard to the type of operation performed, the patients and relatives all agreed and the clinical assessment showed that more favorable results were obtained from "extensive" operations than from "limited" ones. In contrast, patients who had "limited" operations tended to show bigger gains on the social rating scale. This discrepancy is related to the fact that, while more, extensive operations tend to produce greater relief from suffering, they also are more likely to lead to socially crippling defects of personality.

The results obtained support the following conclusions. Operations on the frontal lobes—unless they are very extensive—do not impair the patient's ability to perceive and react appropriately to a painful stimulus, but they produce relief by impairing his ability to elaborate a persisting attitude or mood. The probability that leukotomy will provide relief for a patient with intractable pain depends, first, on the severity of the painful sensations and, secondly, on the nature of the psychological reaction. In patients in whom the pain is not severe and the psychological reaction is largely a depressive or anxious preoccupation with symptoms, the prospects of some degree of relief are high. If pain is severe and frequent, little permanent relief is to be expected. In patients with hysterical tendencies, these may be increased, but, since the anxiety which provokes the hysterical symptoms may be reduced, the total change is often a gain in social adaptation. Operations on the frontal lobe are an unsatisfactory treatment for intractable pain, but, if pain cannot be alleviated by other means, then in carefully selected patients operations of leukotomy type may produce both relief from suffering and an improved social adjustment.

A Controlled Study of the Effects of Leucotomy. A. A. Robin. J. Neurol. Neurosurg. & Psychiat. 21:262-269 (Nov.) 1958 [London].

The author compared the results in 155 women and 43 men treated by leukotomy at Runwell Hospital in Wickford, Essex, England, with those in 198 control patients matched for chronicity (length of stay in hospital), age on admission, sex, and being treated at the same time. Leukotomy did not appear to (1) improve the chances of discharge from the hospital, (2) accelerate discharge, (3) reduce the chances of readmission, (4) delay readmission, (5) reduce the number of readmissions, (6) reduce the total period of readmission, (7) improve hospital behavior as judged by ward level, and (8) significantly increase the death rate. A second leukotomy did not significantly improve the patients' prospects of discharge in relation to the controls. The sex of the patients did not influence the results of leukotomy. "Recovered" patients, i. e., patients who have been discharged from hospital and have not since been readmitted to Runwell or any other mental hospital in England and Wales under the same name, had at least the same level of adjustment in the control group as in the group subjected to leukotomy, and they seemed similar in that they showed the same distribution of diagnoses, ages, and lengths of stay in hospital. No evidence was found for a delayed operative response after leukotomy.

GYNECOLOGY & OBSTETRICS

The Transmission of Transfused Sickle-Trait Cells from Mother to Fetus. N. T. Macris, L. M. Hellman and R. J. Watson. Am. J. Obst. & Gynec. 76:1214-1218 (Dec.) 1958 [St. Louis].

This paper describes a method by which it is ascertained whether intact maternal erythrocytes cross the placental barrier. Donor blood with the sickle-cell trait but without sickle-cell anemia was selected for this purpose. When erythrocytes with the sickle trait are exposed to a decreased oxygen tension, they assume a characteristic sickled configuration which is easily recognized. A group of pregnant women was, therefore, injected with sickle-trait blood, and the blood of their infants was examined for sickle cells. The subjects of this study were 25 Rh-positive pregnant women at or near term. Specimens of their blood were examined for sickle cells, and in all except one none were found. When available, the husband's blood was also examined for sickling. The selection of subjects in this study was governed largely by the blood group of the sickle-trait donor blood that was available. They ranged in age from 17 to 38 years and included 18 Negroes, 4 Puerto Ricans, and 3 whites.

Twenty-one of the subjects were transfused with 500 ml. each of sickle-trait whole blood. In 3 instances the supernatant plasma in 500 ml. of whole blood was removed, allowing the sickle-trait cells to be given in a reduced volume. The elapsed time, between the end of transfusion and delivery, ranged from 40 minutes to 153 hours and 2 minutes. Nineteen of the women were delivered vaginally, and 6 by cesarean section. Whole blood was collected both from the umbilical cord at delivery and from the mother within 12 hours after delivery. Sickle-cell preparations of the mother's and infant's bloods were prepared.

Sickle cells were found in the umbilical cord blood of the newborn infant in 3 of the 25 cases studied. The placenta in each of the 3 cases was normal on gross inspection. The placental passage of sickle-trait cells in 3 of 25 experimental subjects adds to the already existing evidence that in a small percentage of patients maternal red blood cells traverse the placental barrier and are found in appreciable numbers in the fetal circulation. The mechanism of transfer is obscure. While breaks are known to occur in the fetal circulation, the pressure relationships are thought to be such that direct passage must always occur from fetus to mother. Direct transfer of maternal cells against the pressure gradient is not feasible. Furthermore, the venous pressure cannot fall below the amniotic fluid pressure, which is the same as the intervillous space pressure. The only remaining possibility is active transfer by the process of planocytosis, which has been shown to occur for particulate matter. When certain rough assumptions were made from the data, the fetus in at least one instance must have received at least 5 ml. of sickle-trait cells. Should the placenta be unable to distinguish between sickle-trait and normal maternal cells, the transfusion to accomplish this must have been a bit more than 40 ml., which is altogether unlikely. One is left with the assumption that the microvilli distinguish between natural and unnatural maternal cells, engulfing only the latter. The facts of transfer can no longer be denied. The mechanism remains a baffling mystery.

The Nasal Mucus Smear in Toxemias of Pregnancy. E. H. Abou-Shabanah, J. G. Boutselis, W. J. Frajola and J. C. Ullery. Am. J. Obst. & Gynec. 76:1248-1263 (Dec.) 1958 [St. Louis].

Observations indicate that among pregnant women who are apparently normal during early pregnancy there are some who are potentially preeclamptic, and that significantly greater weight gain occurs in the patient with preeclampsia between the 13th and 20th weeks of pregnancy than in the normal or hypertensive pregnant patient. Eclampsia has been known to occur sometimes without the development of proteinuria or hypertension. Although edema is one of the principal signs of the preeclamptic state, it is possible for true preeclampsia to occur with no pitting edema and with only excessive weight gain. This weight gain is usually too rapid to be accounted for by the growth of the fetus or the gravid uterus. Perhaps an intracellular accumulation of fluid occurs in preeclampsia. Healthy pregnant women also have delayed water excretion and some sodium chloride retention, presumably because of increased activity of the adrenal cortical hormones. In the past storage of water and sodium chloride without obvious edema was difficult to understand. Today, with evidence in favor of the ability of sodium to replace intracellular potassium, the latter being excreted, occult edema can be explained. In other words, one expects sometime during the course of preeclampsia–eclampsia to find a change in the ratio between sodium and potassium excreted in body fluids. The study of potassium excretion in the urine revealed no characteristic curve for preeclampsia. In this paper the authors demonstrate the value of the nasal mucous smear in the study of the toxemias of pregnancy.

In a preliminary study, nasal mucous smears were made on 5 patients at the Demerdash Hospital, Cairo University, Egypt—3 in the preeclamptic phase and 2 in eclamptic convulsions. The excretion of sodium and potassium in the nasal and cervical mucus of normal pregnant women was studied in an attempt to relate the sodium and potassium excretion to the fern phenomenon. Some of the mucus, as obtained, was spread on a slide for the fern test, while the remainder was treated with a minimum of dilute hydrochloric acid and water, filtered to remove strands, and the filtrate analyzed for sodium and potassium content by flame spectrophotometry. The nasal mucus from 30 pregnant women, who on admission presented signs and symptoms of late toxemia of pregnancy, was examined. Nasal smears were taken on admission, then hourly in severe cases, and twice daily in others.

Nasal mucous smears were classified on the basis of the presence or absence of arborizations. When arborizations were present, a further classification was made according to whether the pattern showed beaded arborizations (unlinked arborizing crystals) or an atypical fern (deficient or incomplete fern arborization). Oils of different refractive indexes were used to identify the presence of calcium or potassium on the smear. The absence of arborization (negative fern phenomenon) in a smear of nasal mucus is associated with preeclampsia-eclampsia. The sodium-potassium ratio of the nasal mucus of normal pregnant women and of pregnant women with hypertension and/or renovascular disease is greater than 1, whereas in preeclampsia-eclampsia it is reversed. The use of index of refraction oils on smears of nasal mucus will enable the physician to detect preeclampsia by a simple office test. This test also guides him in the management of, and the prognosis for, both mother and fetus.

Management of the Pregnant Diabetic. W. S. Jones. Diabetes 7:439-445 (Nov.-Dec.) 1958 [New York].

Among the 140,665 deliveries at the Providence (R. I.) Lying-in-Hospital in the 31-year period from 1927 to 1957, there were 273 pregnancies in 169 diabetic women. After excluding abortions and dubious diagnoses, there remained 251 viable pregnancies, on which this study is based. The prevalence of prepaid insurance coverage has created a progressive shift from clinic to private patient status. The 93 private deliveries were conducted by 26 different obstetricians, and 43 internists and general practitioners participated in their medical management. This lack of uniformity of control is in marked contrast to that in a teaching hospital. Furthermore, many patients resist long periods of hospitalization desirable in the last trimester, and the community obstetric service is obliged to accept emergency cases and miscellaneous drifters, infrequently seen in specialized centers. This has a devastating effect on fetal loss statistics.

Answers were sought to two questions: What kind of diabetic women lose their babies, and under what circumstances? Fetal loss was investigated in relation to the age of the mother, the age at which she acquired diabetes, and the duration and severity of her diabetes. The great majority of fetal deaths was associated with 3 clinically detectable physiological complications: 1. In the presence of acidosis, the fetal loss was 51%. 2. In women with preeclampsia, 32% of the infants died. 3. In cases in which hydramnios was recorded, the wastage was 37%.

The author feels that progress in improving fetal salvage in diabetes seems painfully slow. The loss over a 31-year span was 28%, and it has remained close to 25% in recent periods. Much of this loss occurs among older women and among those with mild forms of diabetes—patients in whom better results should be achieved. Much of the fetal loss stems from small but costly slips in diabetic control and from debatable obstetric judgment. The author believes that improved fetal salvage will come about, not by emptying the uterus earlier or by doing more cesarean operations, but by paying closer attention to the control of diabetes and toxemia.

Diverticulitis, Sigmoiditis and Perisigmoiditis from Gynecologic Viewpoint. J. A. Abolins. Nord. med. 60:1568-1569 (Oct. 30) 1958 (in Swedish) [Stockholm].

Diverticulitis can cause both diagnostic and therapeutic difficulties. The disease seems to occur more frequently. When a resistance in the small pelvis is found, especially with inflammation, the possibility of diverticulitis, sigmoiditis, or perisigmoiditis should be considered. The history gives valuable information. Usually for a long time before the first consultation there has been constipation, diarrhea, and flatulence. The commonest symptom is abdominal pain on the left side, together with fever. Roentgenologic examination is desirable, but in the acute stage it is not without danger. Often the first roentgenologic examination does not give certain diagnosis. Conservative treatment is advised. The 6 cases of diverticulitis described were observed during a half-year period in patients admitted on the diagnosis of gynecologic disease. Diverticulitis was established at laparotomy or on roentgenologic examination. Treatment was with antibiotics, salazopyrine, and diet. The patients continue free from symptoms after 2 years.

Fetomaternal Leukocyte Incompatibility. R. Payne and M. R. Rolfs. J. Clin. Invest. 37:1756-1763 (Dec.) 1958 [New York].

Isoleukoagglutinins are known to develop primarily in patients who have received many transfusions, but there may also be other stimuli for leukoagglutinin production. Investigators have drawn upon the analogy to Rh antibody formation and have discussed the possibility that fetal leukocyte antigens might act as stimuli to the mother. The studies presented in this paper demonstrate that fetomaternal leukocyte incompatibility may induce leukoagglutinin formation in the mother and suggest that some leukocyte factors, as demonstrated by their corresponding leukoagglutinins, may be genetically transmitted to the offspring. Serums were collected from 3 groups of women. Group 1 included 144 obstetric clinic patients selected with the sole qualification of multiparity; all women had had 4 or more pregnancies. The majority of the women were in the third trimester of pregnancy, while a few were in the second trimester, as it was thought that more easily detectable amounts of antibody might be present in parous women during late pregnancy. Group 2 consisted of 8 patients who were included because they showed varied circumstances in which leukoagglutinins could be found in parous women. The majority of group 2 had Rh antibodies. There was A-O incompatibility between newborn infant and mother in one instance; another patient was referred because of an anemia of unknown origin; and the last had had a febrile transfusion reaction. Group 3, a control series, consisted of 20 healthy women who had never been pregnant and had never received transfusions.

Leukoagglutinins were found in 25 (or 17%) of the 144 multiparous women. They were completely absent in the controls who had never been transfused or been pregnant. The fetus appeared to be the only stimulus for leukoagglutinin production in 18 of the 25 women, since this number had never received transfusions or blood injections. Isoleukoagglutinins of the maternal serums agglutinated the leukocytes of 10 of 12 of the patients' respective newborn infants, and 12 of 13 of their respective spouses, thus suggesting the inheritance by the offspring of the fathers' leukocyte factor. Maternal sensitization to leukocytes appears to develop in a manner analagous to Rh sensitization.

PEDIATRICS

Streptococcal Infection in a School Population: Preliminary Report. D. Cornfeld, G. Werner, R. Weaver and others. Ann. Int. Med. 49:1305-1319 (Dec.) 1958 [Lancaster, Pa.].

Evidence that prompt and continued treatment of streptococcic infections of the throat may greatly reduce the incidence of primary attacks of rheumatic fever has been obtained largely from military establishments, in which groups are at the risk of epidemic transmission of infectious disease, and in which infection may be subjected to epidemiologic studies. The studies presented here aimed to ascertain whether children of school age, the group most vulnerable to rheumatic fever, can be protected from first attacks of rheumatic fever in a manner similar to that found to be effective in military groups. Three schools in south Philadelphia were selected to furnish for study a population of approximately 1,000 children. During the school year, clinical epidemiologic and bacteriological data were obtained from the children and, where indicated from their family contacts. The aim was to determine: (1) the carrier rate of beta-hemolytic streptococci, (2) the rate of clinically manifest streptococcic infection, and (3) the effect of various treatment programs on both the carrier rate and the rate of clinically manifest infection.

In each of the school years, approximately one-half of the children had one or more positive cultures for beta-hemolytic streptococci, regardless of attempts to control carriers by penicillin treatment. The rate of clinically manifest streptococcic infection remained relatively low in all schools, independent of the existing carrier rate or treatment programs instituted. Relatively few of the children with respiratory symptoms had positive cultures for beta-hemolytic streptococci, and even in the group with positive cultures most of the children presented symptoms of undifferentiated respiratory tract illness. Most of the beta-hemolytic streptococci isolated were of group A, but a large percentage of these could not be typed. The poured-plate method of growing streptococci permitted a significantly higher recovery rate than did any enrichment method or direct streaking method tried. In view of the data presented, the authors question the efficacy of the currently popular programs based upon bacteriological culture studies on school children and penicillin treatment for those found to harbor streptococci in their throats.

Spontaneous Perforation of Bile Ducts in Infancy. T. C. Gertz. Ugesk. læger 120:1454-1458 (Oct. 30) 1958 (In Danish) [Copenhagen].

Spontaneous perforation of the bile ducts in infancy is a rare disorder. The first 2 cases of the entity were described by Caulfield in 1936; 8 additional cases have since been published. Spontaneous perforation of the bile ducts in infancy is characterized by mild intermittent jaundice, acholic stools, absence of bile pigment in the urine, gradually increasing distention of the abdomen with ascites, and often bilateral inguinal hernias containing fluid. The case which the author describes in a female infant, aged 4½ months, recently treated in the Rigshospitalet, Copenhagen, is the 11th case to be reported. The spontaneous perforation of the choledochus in this patient probably originated at the age of 5 to 9 weeks. Cholecystocholangiography revealed a perforation in the choledochus. On operation large amounts of bile-colored ascites fluid were found from an abscess under the right liver lobe. The postoperative course after simple drainage of the choledochus was uneventful, and the patient was discharged as well a month later. The disease is usually subacute but can sometimes be acute. In untreated patients it is fatal. It is important to know the disease so that diagnosis can be timely. Operation with simple drainage of the choledochus region has proved curative in most cases. Preoperative cholangiography is a valuable diagnostic aid.

The Development of Prematurely Born Children with Birth Weights or Minimal Postnatal Weights of 1,000 Grams or Less. M. Dann, S. Z. Levine and E. V. New. Pediatrics 22:1037-1053 (Dec.) 1958 [Springfield, Ill.].

The authors report observations on the physical, mental, and social development of 73 children with very low birth weights, born prematurely between

Jan. 1, 1940, and Dec. 31, 1952, who were discharged alive from the premature nursery of the New York Hospital and were examined between October, 1950, and November, 1957. Of the 73 children, 37 were in the statistical birth weight group of from 660 to 999 Gm. (1½ to 2¼ lb.) and 36 weighed 1,000 to 1,280 Gm. (2¼ to 2¾ lb.) at birth, but their weight fell to 1,000 Gm. or less in the neonatal period. At the time of the examination, 32 children had reached the age of at least 4 years, and the oldest child was 10 years old. In 34 families in which there was a full-term brother or sister, 4 years of age or older, these siblings served for comparison. For obvious reasons, these full-term children were not strictly comparable with the premature group, but they had the same parents and essentially the same home environment.

With rare exceptions, physical health of the prematurely born children was good, with a marked paucity of neurological defects. They showed a tendency to catch up in height to normal standards for chronological age, but often not until after 4 years of age. The incidence of eye defects, especially strabismus and myopia, was high. Intelligence quotients showed a wide range from 59 to 142; the average intelligence quotient was 94, and it was significantly below that of 107 found in the 34 full-time siblings examined for comparison. Twelve of the 73 prematurely born children had intelligence quotients below 80; among the 43 of similar birth weight but not available for examination, 19 were known to be mentally retarded, and 5 of these were in institutions. A significantly higher proportion of the children with intelligence quotients above 100 was found among families of higher socioeconomic rating. A suggestive advantage of girls over boys and of white over nonwhite children was noted, though the latter factor was probably secondary to socioeconomic factors. A high incidence of serious maternal complications existed and might well have influenced the outcome, but within the group no relationship was found between lower intelligence quotient and complications of pregnancy and delivery, with the possible exception of toxemia and cesarean section. There was no greater incidence of low intelligence quotient in patients with visual handicaps than in the total group.

An Additional Contribution to the Study of Constitutional Methemoglobin Cyanosis: Description of Two Cases. G. Bono and P. C. Gamalero. Minerva pediat. 10:1076-1082 (Oct. 13) 1958 (In Italian) [Turin, Italy].

The authors report on 2 male children, brothers, 6 and 3 years old, respectively, with cyanosis. Abnormal amounts of methemoglobin were found in the blood of both patients. The condition was manifest on the skin and on the mucous membranes and became marked on fatigue or when the children cried. The first child also presented clubbed fingers, tracheobronchial adenopathy of tuberculous nature, and latent dyspnea; mild dysrhythmia with slow diffused waves was noticed on electroencephalographic examination. Marked erythrocyte fragility was present in both children and in their parents. The patients were treated with large doses of vitamin C given cyclically by intravenous injection and by mouth for prolonged periods of time.

DERMATOLOGY

Treatment of Persistent Acne in Women with 17 Alpha Hydroxyprogesterone Caproate (Delalutin): A Preliminary Report. K. C. Baker. J. Invest. Dermat. 31:247-250 (Nov.) 1958 [Baltimore].

Seventy-six women, between the ages of 15 and 36 years, with acne, 69 of whom had a definite history of premenstrual exacerbation of the eruption, were treated with 17-alpha-hydroxyprogesterone caproate (Delalutin), an esterified derivative of the naturally occurring progestational hormone. The group included patients with 4 different clinical types of acne; a diagnosis of acne vulgaris was made in 37 women, of acne cystica in 19, of acne rosacea in 3, and of acne sebacea in 17 patients. A single dose of 125 mg. (1 cc.) of this long-acting drug was injected deeply into the gluteal muscle between the 14th and the 18th day after the onset of menstrual flow. Injections were given for a total of 2 to 8 months during the course of the study. Standard therapeutic measures in current use had failed to control the manifestations of acne in these patients. A good to excellent response, as indicated by the clearing of existing lesions and by the prevention of new lesions, was achieved as a result of treatment with this progestational agent in 64 of the 76 patients. A single injection of the steroid ester given once a month and repeated 2 to 6 times thus considerably improved the appearance of the skin. In the dosage administered, hydroxyprogesterone caproate was well tolerated. An alteration in the menstrual pattern (with scanty menses) was observed in one patient during the course of therapy. When the hormone injections were discontinued, however, the menstrual flow again assumed its usual characteristics.

The prolonged effect of the progestogenic compound (10 to 14 days) is thought to resemble the sustained action of the continuous endogenous production of progesterone by the corpus luteum. In comparison, free progesterone has a relatively brief effect (2 to 3 days). The availability of hydroxyprogesterone caproate with a prolonged progestational activity makes possible a physician-controlled regimen which maintains a high progesterone level in rhythm with the normal menstrual cycle. The reported data suggest that hydroxyprogesterone caproate should be given an extensive trial either alone or in conjunction with other systemic and local measures as a therapeutic agent in women with persistent acne.

A Localized Outbreak in New York of Tinea Capitis Due to Trichophyton Violaceum: Observations with Special Reference to Mixed Infections of the Scalp. S. A. Rosenthal, D. Fisher and D. Furnari. A. M. A. Arch. Dermat. 78:689-691 (Dec.) 1958 [Chicago].

Infection of the scalp with Trichophyton violaceum is a rare finding in the United States, although it is common in other areas of the world. The observation of 2 species of fungi simultaneously infecting the same scalp is likewise rare. This paper reports on a localized outbreak of tinea capitis due to T. violaceum, with observations on mixed fungous infections of the scalp, in the Willowbrook State School, Staten Island, N. Y. (for mentally retarded persons). T. violaceum was isolated from 44 of 88 subjects with clinical tinea capitis. A surprisingly large number of mixed fungous infections of the scalp was observed. Of 71 subjects with culturally proved tinea capitis, 33 (46%) showed a mixed scalp infection, with 4 of these each yielding 3 species of fungi.

The clinical picture seen in this series of scalp infections with T. violaceum did not usually show the classic, "black dot" type of morphology. Infected areas showed various degrees of scaling and erythema with broken-off hairs several millimeters long. Often normal-appearing hairs were also present in these areas. The source of the T. violaceum outbreak in this state school is unknown. The close personal contact necessitated by institutional life may well be a cause of considerable dissemination of fungous diseases due to species which otherwise rarely produce disease in the United States.

Skin Lesions Caused by Chlorpromazine. W. G. van Ketel, J. J. Morriën and H. H. Lenstra. Nederl. tijdschr. geneesk. 102:1799-1804 (Sept. 13) 1958 (In Dutch) [Amsterdam].

Published reports show that chlorpromazine sometimes produces skin lesions of the cutaneous vascular type, particularly in patients treated with large doses. The epidermis shows no pathological changes, and the skin lesions rapidly disappear after chlorpromazine therapy is discontinued. After recovery it is often possible to resume treatment with chlorpromazine in smaller doses. It has also been pointed out that it is not always necessary to stop the administration of chlorpromazine, for the skin eruption may subside if the dose is only reduced, or even if it is not changed at all. Tests have revealed that exposure to sunlight may intensify eruptions brought on by chlorpromazine.

Cutaneous lesions that result from sensitization to chlorpromazine by external contact present a different problem than the eruptions caused by medication. An allergic contact dermatitis localized chiefly on the fingers and around the eyes may develop in nursing personnel handling tablets or solutions of chlorpromazine. The authors found that 7 of 62 members of the nursing staff in a small hospital had contact dermatitis; in 5 of these patients the dermatitis was due to chlorpromazine, in 1 chiefly to streptomycin, and in 1 to penicillin. The patch test is valuable in the diagnosis of contact eczema. The onset of the contact dermatitis is usually more delayed, but its prognosis is less favorable than that of the eruption resulting from treatment. No general statement can be made with regard to the influence of exposure to sunlight on the contact dermatitis. Although in one patient such exposure caused an exacerbation, in others the lesions developed in winter, and patch tests combined with sun exposure or ultraviolet irradiation could not be carried out. Repetition of sensitivity tests showed a lessening of sensitivity in some of the patients. A study was made of the most suitable concentrations for testing sensitivity reactions. Cross sensitivity for chemically related preparations, notably promazine, could not be established.

THERAPEUTICS

A Study of the Effectiveness of Certain Anorexigenic Agents. J. F. Fazekas, W. R. Ehrmantraut and J. Kleh. Am. J. M. Sc. 235:692-699 (Dec.) 1958 [Philadelphia].

The authors conducted double-blind studies of the anorexigenic effects of phenmetrazine hydrochloride, a combined preparation of dextro amphetamine sulfate and amobarbital, and a placebo. Phenmetrazine hydrochloride and a placebo were given to, and their effects compared in, a group of 106 obese, mentally normal persons, and, in order to obviate insofar as possible the influence of suggestion, all 3 agents were given to, and their effects compared in, a group of 43 obese, mentally deficient persons. The study was terminated after 28 weeks. In both the mentally alert and the mentally deficient persons, there was a significant reduction of weight with phenmetrazine but no significant change during the placebo administration. Subjective undesirable side-effects, which were evaluated only among the mentally normal persons, disclosed no apparent difference between phenmetrazine and the placebo. In the mentally deficient group, the weight loss induced by dextro amphetamine sulfate was similar to that obtained with phenmetrazine. It is postulated that these drugs act primarily in subcortical areas, probably by influencing localized neurohumoral activity. In view of the almost certain influence of the cortex and spinal cord, as well as the subcortex, on appetite, it should not be surprising that there is considerable variability in individual response to anorexigenic agents.

The Clinical Investigation of a Codeine Resin Complex: A Long Acting Analgesic for Oral Administration. L. J. Cass and W. S. Frederick. New England J. Med. 259:1108-1111 (Dec. 4) 1958 [Boston].

The search for an improved analgesic that can provide effective and sustained relief of pain without appreciable side-effects prompted this study. Experiments in animals have shown that the toxicity of codeine is substantially reduced when it is administered as an ion-exchange resin complex, and also that the analgesic action of the resin complex is potentiated by the addition of certain amines that in themselves have little or no pain-suppressing activity. It seemed desirable to undertake an evaluation of several formulations of the codeine resin complex with other compounds and compare them with a standard preparation, such as mixtures of codeine and acetylsalicylic acid, phenacetin and caffeine citrate.

Eleven analgesics were evaluated in 3 separate clinical experiments on 65 patients with various painful conditions, their ages ranging from 40 to 60 years. Data obtained from a total of 24,640 observations showed that the codeine-methyl-ortho-tolyl-quinazolone resin complex is an effective, long-acting analgesic, in which the synergistic action of the quinazolone derivative makes it possible to reduce the daily total dosage of codeine required to control moderate pain. It was demonstrated that this drug has a greater pain-suppressing effect—for 12 hours after a single dose—than standard codeine combined with acetophenetidin, aspirin, and caffeine.

Experimental and Clinical Research on the Action of Soybean Oil on Cholesterolemia. R. Wolff, R. Herbeuval, G. Cuny and others. Presse méd. 66: 1706-1708 (Nov. 1) 1958 (In French) [Paris].

Alimentary lipids play a large part in the regulation of cholesterolemia. Recent studies have distinguished the action of fats of vegetable origin from that of fats of animal origin. The suppression of animal fats and generally fats rich in saturated fatty acids lowers the level of blood cholesterol. Vegetable oils introduced into the diet in about 40 to 50% of caloric needs exert a hypocholesterolemic action. This action is related to the richness of the fats in unsaturated fatty acids. It is not as yet agreed as to the nature of the unsaturated fatty acids responsible for lowering the cholesterol level. The unsaturation of oils is due to the presence of fatty acids in one or several combinations. These combinations are measured by the iodine index. It was found that the iodine index of soybean oil is high (higher than that of corn oil). Soybean oil contains 4% of vegetable sterols of the beta-sitosterol type. This sterol exerts a hypocholesterolemic action in rabbits and in man by checking the intestinal absorption of cholesterol of exogenous origin. A priori, soybean oil is susceptible of having a hypocholesterolemic action by its degree of unsaturation and by its richness in beta-sitosterol.

The action of soybean oil from the experimental and clinical viewpoints was studied in the laboratory of biological chemistry and in the clinic for diseases of older patients at the Medical School of Nancy. Five lots of 6 to 8 rabbits were given a special feeding with 3 ml. of soybean oil per kilogram of body weight for a period not exceeding 8 days. After this administration there was noted a drop in the level of blood cholesterol, which reached 23 to 31% of the initial value and occurred as early as the next day. Research on man was carried out by studying 15 men whose ages ranged from 50 to 70 years. All except 2 had different manifestations of arteriosclerosis. Nine had arteriosclerotic fundus oculi, with lesions of the capillaries in the retina and cholesterol deposits. Six had arterial hypertension. At the beginning the level of blood cholesterol was high in all subjects—from 2.42 to 4.50 Gm. They were put on a diet with the administration of 1.5 cc. of soybean oil before each of the 2 main meals. In 6 subjects for whom the diet was of short duration (6 to 11 days), a constant fall in the level of total cholesterol was noted. The average fall was to 16% of the initial value. In 9 subjects the administration of soybean oil was of long duration (an average of 63 days). The findings regarding cholesterol level in this group were heterogeneous and difficult to interpret. Despite the presence of large amounts of unsaturated fatty acids of the "essential" type in soybean oil, the action of this oil on cholesterolemia is questionable. Factors other than the unsaturation of fats must intervene in the regulation of blood cholesterol.

An Inter-Relationship Between Ascorbic Acid and Cyanocobalamin. E. V. Cox, R. Gaddie, D. Matthews and others. Clin. Sc. 17:681-692 (Nov.) 1958 [London].

Deficiency of cyanocobalamin, vitamin B_{12}, is closely associated with megaloblastic anemia, and a deficiency of ascorbic acid gives rise to scurvy. The authors cite previously reported observations that suggest an association between these two vitamins, but as yet definite evidence of this in an adequate number of patients is lacking. The investigations reported in this paper were undertaken to determine whether there was indeed any relationship between B_{12} and ascorbic acid. The effect of B_{12} administration on the plasma concentrations of ascorbic acid before and after an intravenous injection of 250 mg. of sodium ascorbate was studied in patients with pernicious anemia, in adults with celiac disease, and in patients with regional ileitis. The patients with low serum B_{12} levels had significantly lower plasma ascorbic acid levels than normal controls.

The rate of disappearance of the injected sodium ascorbate was increased in the state of vitamin B_{12} deficiency—in patients with pernicious anemia, 38.7%; in adults with celiac disease, 39.3%; and in patients with regional ileitis, 36.0%—compared with 24.4% in healthy subjects. After B_{12} therapy the abnormal ascorbic acid metabolism was corrected in patients with pernicious anemia and improved in adults with celiac disease. No change was noted in those with regional ileitis. The effect in pernicious anemia and in celiac disease of adults was masked in those partaking of diets containing a plentiful or a grossly deficient supply of ascorbic acid. In regional ileitis, the lack of effect of B_{12} was attributed to the activity of the underlying disease; a significant correlation was noted between the levels of seromucoids and plasma ascorbic acid. The effect of B_{12} deficiency on ascorbic acid metabolism was greater when the deficiency was associated with a megaloblastic anemia in patients with pernicious anemia and celiac disease of adults than it was in similar patients with a normal erythropoiesis.

Folic Acid and Cyanocobalamin in Pernicious Anaemia. E. V. Cox, M. J. Meynell, W. T. Cooke and R. Gaddie. Clin. Sc. 17:693-699 (Nov.) 1958 [London].

The observation that vitamin B_{12} deficiency can occur without megaloblastic anemia has been noted repeatedly, and it is difficult to explain the hematopoietic defect of pernicious anemia solely on the basis of B_{12} deficiency. A deficiency of folic acid would appear to be of little therapeutic significance, since supplementary folic acid is rarely required in pernicious anemia. The therapeutic activity of folic acid and the lack of anemia in some patients with B_{12} deficiency, however, indicate the possibility of a relationship between these compounds. In this study the authors investigate the metabolism of folic acid in pernicious anemia and observe the effect of B_{12} therapy. Folic acid (5 mg.) was given intramuscularly to 20 normal subjects, 23 hospital patients with no evidence of neoplasm or renal disease, 10 patients with pernicious anemia in relapse, and 10 with pernicious anemia in remission. The urine was collected for 24 hours after the test dose, and an aliquot of each specimen was assayed in duplicate with Streptococcus faecalis to estimate the folic acid content.

The patients with pernicious anemia in relapse were given test doses of folic acid, and the urinary excretion of folic acid was determined on alternate days over a period of at least 14 days. Giving the test dose on alternate days prevented significant overlap in the increased urinary excretion of folic acid. The administration of cyanocobalamin (250 or 1,000 mcg. given intramuscularly daily for 10 days) was commenced in 8 patients after the third folic acid injection and after the first injection in the other 2. The high dosage of vitamin B_{12} was given to obtain saturation as soon as possible. These experiments were controlled by performing similar folic acid excretion tests on alternate days in 3 normal subjects and in 2 patients in complete remission induced by vitamin B_{12}. Two patients with pernicious anemia were studied in the same way as the other patients with this disease, but, instead of folic acid, test doses of 3 mg. of leucovorin (folinic acid) were used. The urinary excretions of folic acid and folinic acid were assayed with Str. faecalis and Leuconostoc citrovorum together with a differential assay.

The results of the various tests are presented in tables, including the excretion of material with only folic acid-like activity (pteroylglutamic acid [P. G. A.]) and that assayable with L. citrovorum (citrovorum factor [C. F.]) in the 2 patients given leucovorin test doses. Summarizing their observations, the authors say that, with a folic acid excretion test, evidence of a deficiency of folic acid was found in 5 out of 10 patients with pernicious anemia. The degree of unsaturation appeared to be slight, and probably does not contribute to the dyshematopoiesis of pernicious anemia. In patients treated with cyanocobalamin, a reduced excretion of P. G. A. and C. F. occurred after administration of either 5 mg. of folic acid or 3 mg. of leucovorin. The changes in the nature and rate of the hematopoiesis were not solely responsible for this fall, since in all but 2 patients they occurred after the reticulocyte peak.

Failure of Ristocetin Therapy in Three Cases of Staphylococcal Sepsis with Bacteremia. L. A. Rantz and E. Jawetz. New England J. Med. 259:963-966 (Nov. 13) 1958 [Boston].

Ristocetin is a new antimicrobial agent produced by Nocardia lurida, of large molecular size and active against gram-positive bacteria. It has been stated to be effective in the treatment of enterococcic and staphylococcic endocarditis. The manufacturer's brochures suggest that it is bactericidal for staphylococci and that patients with severe disease caused by these organisms may be expected to benefit from its administration. Studies in vitro by one of the authors, described here, and by others previously demonstrate that this is not a bactericidal drug, and very few published data are available to substantiate its clinical efficacy. The authors present the histories of 3 patients with staphylococcic sepsis with bacteremia whom they treated with ristocetin. Bacteremia persisted in each during therapy, and clinical improvement failed to occur. The serum of 2 patients was bacteriostatic and bactericidal for the causative organism at the very time that it could still be isolated from the blood. Clinical improvement did not occur in any patient, and in one there was a substantial deterioration in the condition while 2 Gm. of ristocetin was being administered daily.

These treatment failures in patients with infections caused by staphylococci apparently as sensitive to the action of ristocetin in vitro as strains examined by other investigators, and, in fact, inhibited and killed by the serum of the patients during treatment, suggest that a serious and unknown defect in the mode of action of this drug must protect the micro-organism from its effects. It was first thought that this might be due to serum binding, but this could not be demonstrated in vitro. The complete failure of response in 3 patients with staphylococcic sepsis does not suggest that it will be of great value in the management of this disease. Better results were obtained in each case by appropriately selected combinations of other antimicrobial agents, and the infection was eradicated in 2 by this technique.

The Treatment of Constipation with the Use of Antibiotics. A. Ravina. Presse méd. 66:1649-1650 (Oct. 25) 1958 (In French) [Paris].

The author found that several antibiotics, especially tetracycline and neomycin, had results superior to those of ordinary laxatives in the treatment of constipation and can even cure it. Posology is related to results obtained. The author suggested 1 Gm. of tetracycline daily for 5 to 7 days, 500 mg. for the same length of time, and then 250 to 500 mg. twice a week. Effects were usually seen 3 or 4 days after the beginning of treatment. It was rarely necessary to continue treatment for more than a month. Other antibiotics used were Rovamycin (in moderate initial doses), Oleandomycin, Cathomycin, Aureomycin, and Terramycin. When diarrhea occurred, 5 to 10 Gm. of bismuth subnitrate and small amounts of antispasmodic drugs were added to the treatment. Antibiotic medication for constipation was well tolerated. Long experience showed that fears of digestive disturbance due to bacteriolytic substances and of the appearance of a microbial resistance which could impair the action of antibiotics in case of serious infections were groundless. Doses were small enough so that digestive disorder rarely followed. The types of constipation that accompany acne rosacea and dolichocolon or megacolon were especially responsive to this treatment. Cures were complete and prolonged. Even after a short-term antibiotic treatment the volume of feces was considerably increased in a large number of cases.

Further research is needed to define the mode of action of this antibiotic therapy. It is suggested that the effect is due to a modification of the intestinal peristalsis in those patients who have a more serious colonic stasis than was presumed. The author believes that the explanation can more reasonably be based on profound modifications of the intestinal flora.

PATHOLOGY

Hemorrhagic States Secondary to Intravascular Clotting: An Experimental Study of Their Evolution and Prevention. G. D. Penick, H. R. Roberts, W. P. Webster and K. M. Brinkhous. A. M. A. Arch. Path. 66:708-713 (Dec.) 1958 [Chicago].

The paradoxical sequence of clotting followed by hemorrhage develops in certain hemorrhagic complications of pregnancy, surgical trauma, burns, etc. This investigation was conducted to determine whether animals with comparably defective clotting system would be protected from the effects of intravenously administered thromboplastin. The responses of these animals to injected thromboplastin were compared with those of normal control dogs. Crude tissue extracts, which are regarded as "complete" thromboplastin, were injected into 2 normal and 2 hemophilic dogs. Shortly all the animals exhibited minor convulsive movements, hyperpnea, cyanosis, nystagmus, and excessive salivation. The reaction in the hemophilic dogs was less severe and less prolonged than that in the normal animals. All the dogs exhibited thrombocytopenia, hypofibrinogenemia, hypoprothrombinemia, and depressions in the antihemophilic activity of the plasma. These responses were diminished or were nonexistent in dogs with hypocoagulable blood. A similar reaction took place after injection of ultracentrifuged preparations of thromboplastin, which are regarded as "partial" thromboplastin, into a normal and a hemophilic dog. After injection the normal dog showed signs of respiratory difficulty, hyperkinesis, excessive salivation, and tachycardia. Prothrombin concentration was not appreciably altered in either animal. The fibrinogen level decreased in the normal dog but did not change significantly in the hemophilic dog. Depression in the antihemophilic activity of the plasma occurred in the normal dog. Thromboplastin injection prolonged the prothrombin time of the plasma in 4 other normal dogs; no changes were noted in the hemophilic dog.

Partial thromboplastin was injected into each of 4 dogs treated with bishydroxycoumarin (Dicumarol) and into 2 normal dogs. Both normal animals developed respiratory difficulty, hyperkinesis, tachycardia, and pupillary dilation. The animals treated with Dicumarol showed no overt response. In the normal dogs transient thrombocytopenia, hypoprothrombinemia, hypofibrinogenemia, and secondary hemophilia were manifest. These changes were less pronounced in the animals treated with Dicumarol. Partial thromboplastin was injected into 4 dogs to which chloroform had been administered by inhalation 48 hours earlier. Two normal control dogs were studied at the same time. The normal animals again showed reaction signs similar to those described previously. The chloroform-treated animals, even when given up to 6 times as much thromboplastin as the normal dogs, showed no apparent response. Chloroform administration alone had produced low levels of prothrombin and of fibrinogen and depressed the antihemophilic activity of the plasma in all 4 dogs to about 45% of the levels before chloroform treatment. These findings indicate similarity between the response to injected thromboplastin and the reactions known to occur during in vitro coagulation. They tend to support the concept that the hemorrhagic states in disorders associated with circulating thromboplastic tissue products probably result from widespread intravascular coagulation and concomitant consumption and depression of many clotting factors.

Staphylococcal Infection Resistant to Chloramphenicol, Erythromycin, and Novobiocin: Effect of Antibiotic Combinations on the Emergence of Resistant Strains. M. Barber, A. Csillag and A. J. Medway. Brit. M. J. 2:1377-1380 (Dec. 6) 1958 [London].

In an attempt to combat the adaptability of Staphylococcus organisms to antibiotics, the authors introduced into a large general hospital in London a policy for the control of antibiotics, the essential items of which were abandonment of penicillin, except in certain wards of the hospital, and use of 2 antibiotics in combination wherever possible and always when erythromycin or novobiocin was used. The antibiotic sensitivity of all strains of Staphylococcus pyogenes var. aureus isolated from patients with infectious diseases in the hospital was studied during 6 months before the introduction of this policy in April, 1958, and for 6 months afterwards.

Analysis of erythromycin-and-chloramphenicol-resistant infections showed evidence of cross-resistance between these two antibiotics. Of 23 erythromycin-resistant strains, 11 came from patients who had been treated with chloramphenicol; 8 of the 11 patients had been given chloramphenicol in combination with erythromycin and 3 had received chloramphenicol without erythromycin. Moreover, 8 of the erythromycin-resistant strains also showed resistance to chloramphenicol, although in 2 cases the patient had been treated with erythromycin but not chloramphenicol. No such cross-resistance was noted between erythromycin and novobiocin, and of 108 patients treated with this combination, none yielded a Staphylococcus organism resistant to erythromycin, although from 2 of these patients strains resistant to novobiocin were isolated. These findings emphasize the danger of erythromycin-resistant infection becoming a hospital problem if the unrestricted use of erythromycin is permitted. Since there is evidence of cross-resistance between erythromycin and chloramphenicol, combined treatment with these 2 antibiotics offers no solution. Since novobiocin, like erythromycin, has the defect that staphylcocci readily become resistant to it, both should be used sparingly, and neither except in combination with the other or with another chemotherapeutic agent.

Two Serological Tests for Staphylococcal Infection. A. G. Towers and G. P. Gladstone. Lancet 2:1192-1195 (Dec. 6) 1958 [London].

Serums obtained from 156 patients, 83 of whom had staphylococcic infections and 73 had other infections, were examined for their content of anti-Panton-Valentine (P.V.) leukocidin during the course of infection, and the results were compared with those of anti-alpha-hemolysin tests. Of the 83 patients, 69 had osteomyelitis, 6 had tuberculous sinuses secondarily infected by staphylococci, and 8 had other stapyhlococcic infections. Of the 73 patients, 22 had bone and joint tuberculosis, and 51 had miscellaneous nonstaphylococcic infections. A rise of titer of anti-alpha-hemolysin was found in only 27 (33%) of the 83 patients with staphylococcic infections, whereas the titer of anti-P.V.-leukocidin was raised in 68 (82%) of the 83 patients. On the other hand, 12 (17%) of the 73 patients with other infections had an increased anti-P.V.-leukocidin serum level, whereas none of them had an increased anti-alpha-hemolysin serum level. A combination of these 2 serologic tests is of diagnostic value, particularly in patients with deep-seated infection from whom no organisms have been isolated, because the organisms often multiply in sites from which recovery is difficult, such as spinal lesions.

Seminiferous Tubule Dysgenesis (Klinefelter's Syndrome) in Identical Twins. D. A. Holub, M. M. Grumbach and J. W. Jailer. J. Clin. Endocrinol. 18:1359-1368 (Dec.) 1958 [Springfield, Ill.].

Seminiferous tubule dysgenesis (Klinefelter's syndrome) was proved by testicular biopsy in 17-year-old identical twins who presented with the typical clinical features of the syndrome. Female nuclear chromatin patterns were present in the Leydig cells and in buccal mucosal smears of both patients. The identity of the twins was established by means of reciprocal homografts, blood antigen studies, dermatoglyphics, and the history of a single placenta. The principal theories concerning the etiology of this syndrome are briefly reviewed. It is concluded that concordance for seminiferous tubule dysgenesis in identical twins in the light of previous evidence supports the concept that a genetic predisposition exists in this disorder.

ANESTHESIA

Procaine Sensitivity: The Relationship of the Allergic Eczematous Contact-Type to the Urticarial, Anaphylactoid Variety: The Use of Xylocaine in Procaine-Sensitive Individuals. A. A. Fisher and H. M. Strum. Ann. Allergy **16**:593-598 (Nov.-Dec.) 1958 [St. Paul].

The authors found that allergic eczematous sensitivity to procaine, besides being an occupational hazard of the dental profession, is fairly common in the general population. They found 36 patients who showed strongly positive reactions to patch tests with 2% aqueous solution of procaine hydrochloride. Recently they were able to confirm the observations of others that many individuals who have allergic eczematous sensitivity to products of the group embracing paraphenylenediamine, benzocaine, and para-aminobenzoic acid frequently show cross-reactions to procaine. Since paraphenylenediamine and benzocaine are among the more common and most potent sensitizers, it becomes apparent that procaine sensitivity may become established in many patients who have never had actual topical contact with procaine. In addition, it must be remembered that procaine is the most widely used local anesthetic. While it is generally admitted that procaine frequently causes eczematous contact allergy, there seems to be no agreement as to the frequency with which it causes urticarial anaphylactoid allergy. In this paper the authors describe experiments carried out to obtain more accurate information concerning the hazards of the injection or ingestion of procaine in patients with allergic eczematous contact-type sensitivity to procaine.

Twenty patients with allergic eczematous sensitivity to procaine were subjected to scratch and intradermal tests, subcutaneous injections, and ingestion of procaine. None of these patients showed immediate local wheal reactions to these tests, and none had general urticarial or anaphylactoid reactions. As a rule, it would seem that allergic eczematous sensitivity to procaine is not accompanied by the vascular, anaphylactoid allergy, certainly not to any notably high degree. Xylocaine has proved an excellent substitute for, and does not cross-react with procaine. Dentists with eczematous sensitivity to procaine can use Xylocaine without skin reaction. Although urticarial anaphylactoid sensitivity rarely accompanies eczematous sensitivity to procaine, it would nevertheless seem wise to use Xylocaine for local anesthesia in all persons sensitive to procaine.

Clinical Evaluation of a New Ultrashort-Action Oxygen Barbiturate for Intravenous Anesthesia. R. Weyl, B. Unal and Y. Alper. Surg. Gynec. & Obst. **107**:588-592 (Nov.) 1958 [Chicago].

The authors report clinical observations on 200 unselected patients in whom anesthesia was induced with the new ultrashort-acting oxybarbiturate, methohexital sodium, also known as compound 25398. Chemically it is 1-methyl-5-allyl-5 (1 methyl-2-pentynyl) sodium barbiturate. It is a white crystalline solid which is easily soluble in water. It is stable in aqueous solution at 5 C for 1 year and at 25 C for 6 months. The pH ranges between 10 and 11. Preliminary studies carried out by others on cats, mice, rabbits, monkeys, and dogs showed the compound to be 3 times as potent and one-half as long in action as thiopentobarbital (thiopental sodium) and much less likely to show accumulation. The compound did not produce venous irritation or hemolysis during these animal experiments.

The authors found that in the 200 patients the new ultrashort-acting methohexital sodium provided smooth rapid induction, adequate maintenance, and prompt awakening with the use of either a 1% solution for intermittent intravenous injection or a 0.2% solution for intravenous drip. The required doses of this drug are small as compared with those of the thiobarbiturates. The drug seems to be metabolized quickly. It supplies good jaw relaxation, so that a pharyngeal airway can be introduced early. Laryngospasm did not occur in this series. The compound provided an adequate state of analgesia; this was best achieved by the slow-drip method. The compound could be used in connection with the usual inhalants and relaxants. No convulsions occurred in this series, and no venous irritation was noted at the site of injection. Compound 25398 seems to be a safe agent in the hands of the experienced anesthetist. It deserves further evaluation.

BOOK REVIEWS

Penicillin. By Harold L. Hirsh, M.D., and Lawrence E. Putnam, M.D. Foreword by Harry F. Dowling, M.D. Antibiotics monographs no. 9. Under editorial direction of Henry Welch, Ph.D., and Féliz Martí-Ibáñez, M.D. Cloth. $4. Pp. 148, with 9 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22; Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

The authors of this monograph have imparted a wealth of highly practical information obtained over a 15-year period of firsthand experience with penicillin. The slant of the book is clinical rather than pharmacological. After a brief historical introduction the antimicrobial spectrum of penicillin is discussed. This chapter identifies those areas in which penicillin is of proved value and points out those infections against which it is clearly ineffective and hence not indicated. Practical suggestions are also given for reducing the incidence of hospital-acquired infections due to penicillin-resistant strains of staphylococci. The clinical aspects of the pharmacology and toxicity of penicillin are briefly but competently presented. The chapter on dosage forms contains useful information on the characteristics of the diverse commercial preparations. The remainder of the book is devoted to a discussion of the use of penicillin in specific infections known to respond to its antimicrobial action. Each section is prefaced by a brief characterization of the particular disease and is followed by recommendations as to the preparation of choice, preferred route of administration, and proper dosage. There is a subject index and a bibliography. Since penicillin is used in practically all branches of clinical medicine, this monograph should be a valuable reference source as well as a manual of therapy for all physicians.

Urology in General Practice. By Frank Coleman Hamm, M.D., M.S., F.A.C.S., Professor of Urology, Department of Surgery, State University of New York Downstate Medical Center, Brooklyn, and Sidney R. Weinberg, M.D., F.A.C.S., Assistant Professor of Urology, Department of Surgery, State University of New York Downstate Medical Center. Paper. $6. Pp. 293, with 259 illustrations [drawings] by Elizabeth Cuzzort. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1958.

The authors state that, after using this book for a year in their classes at the State University of New York, they have been encouraged by the response of students and other teachers to make it available for wider distribution. Although the book is paper-backed the print and paper are excellent and the illustrations are clear and instructive. The aim of this book is to introduce the medical student and the resident to the field of urology, and to provide a ready reference in the subject for those in other branches of medicine and surgery. The principles of management presented are generally accepted. The material is well arranged and adequately illustrated. This is one of the best of many similar texts on urology which have been published in the United States in the past three years.

The Ecology of the Medical Student: Report of the Fifth Teaching Institute, Association of American Medical Colleges, Atlantic City, New Jersey, October 15-19, 1957. Edited by Helen Hofer Gee and Robert J. Glaser, with assistance of Planning Committee. Editorial coordination by E. Shepley Nourse. Published as part 2 of Journal of Medical Education, October, 1958. Cloth. $3. Paper. $2. Pp. 262, with illustrations. Office of Director of Research, Association of American Medical Colleges, 2530 Ridge Ave., Evanston, Ill., 1958.

In the introduction to this comprehensive report Dr. G. P. Berry points out that "becoming a good doctor is one of the most difficult things in the world." The Institute on the Ecology of the Medical Student focused attention on the various stresses that influence the growth and development of the modern physician. The first part of the report treats the characteristics of medical schools and medical students, dealing with the diversity of values and objectives in medical education and the implications of this diversity. The need for intelligent planning in medical education is stressed as well as the need for research into personality development in interactions with the medical school environment. The second section points up certain factors affecting medical students such as the educational environment, noncurricular factors, and student counseling.

The third section presents interesting data on sociological contributions to the study of the medical student, presenting the procedures for the sociological study of the value climate of medical schools, a commentary on medical education in the social sciences, and an analysis of the development of professional attitudes and capacities. The final section deals with educational patterns in medicine today. It presents new directions in programs of medical education, traditional as opposed to novel approaches to medical education, and the place of the student in the British pattern of medical education. This report is a storehouse of valuable material of vital interest and concern to educators in general, as well as to those specifically concerned

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

with medical education. At this transitional stage of medical education the sociological contributions to the problem as reported in this volume are of particular importance.

Practical Leads to Puzzling Diagnoses: Neuroses That Run Through Families. By Walter C. Alvarez, M.D., D.Sc. Cloth. $9. Pp. 490. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada; Pitman Medical Publishing Company, Ltd., 39 Parker St., London, W. C. 2, England, 1958.

The author briefly summarizes his purposes and objectives as follows: "In this book I describe the symptoms and the syndromes which I found bothering 574 relatives of the psychotic and the alcoholic and 99 relatives of the epileptic. A number of these troubles appeared in such high percentages of the cases that they represent minor equivalents of psychosis and epilepsy. Certain it is that in the families with a poor nervous inheritance I have kept finding a remarkable amount of chronic and often life-long nervous illness, with constitutional inadequacy, neurocirculatory asthenia, hypochondriasis, unemployability, alcoholism and the habit of illness. I am left with the strong impression that these tendencies to illness are inherited." Even though the author professes his conclusions to be only impressions, his fervor makes him write as though it is an established fact that descendants of families with mental illness and alcoholism pass defective genes for the nervous system to their offspring. Environment is so casually mentioned that one has to retain many reservations regarding the authoritativeness of the context of the book. The author's list of symptoms of the relatives of the mentally ill includes practically every symptom of which patients can complain. He does not compare these with the percentages of these symptoms of which relatives of patients with carcinoma, heart disease, diabetes, or multiple sclerosis might complain. Over half of the symptoms which he lists occurred in 5% or less of the relatives, which hardly seems to be statistically significant. One's primary impression is that the book is medical fiction and has to be read with many questions in mind. It is doubtful that there is enough established fact in the text to be of much aid in resolving the puzzling problems of clinical practice.

Poliomyelitis: Papers and Discussions Presented at the Fourth International Poliomyelitis Conference. Compiled and edited for International Poliomyelitis Congress. Cloth. $7.50. Pp. 684, with 422 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1958.

The Fourth International Poliomyelitis Conference was held in Geneva, Switzerland, in 1957. As was the case after the preceding conferences the demand for a permanent record of the papers and discussions necessitated the publication of this book. It is dedicated to Franklin D. Roosevelt and Prof. Edmond Grasset, both dead. It is to be hoped that the subject itself will enter the realm of past history soon. At this conference interest was centered on vaccination against poliomyelitis, enteric viruses that cause poliomyelitis-like diseases, cultures of mammalian cells, new diagnostic techniques, group and home care of patients with poliomyelitis, and the treatment of the severely stricken. The book is well illustrated with photographs and diagrams. Many of the papers have summaries and lists of pertinent references, and a general summation is presented at the end. The book is well printed and contains an index.

General Ophthalmology. By Daniel Vaughan, M.D., Assistant Clinical Professor of Ophthalmology, University of California School of Medicine, San Francisco, Robert Cook. M.D., Clinical Instructor, Department of Ophthalmology. University of California School of Medicine, and Taylor Asbury, M.D., Assistant Professor of Ophthalmology, College of Medicine, University of Cincinnati, Cincinnati, Ohio. Paper. $4.50. Pp. 328, with illustrations by Ralph Sweet. Lange Medical Publications, Los Altos, Calif., 1958.

From the first pages, where the differential diagnosis of common causes of the inflamed eye is clearly outlined, through the excellent index and selected bibliography the authors present a concise, up-to-date outline of ophthalmology. This work should be of great value in the diagnosis and treatment of eye diseases, not only to the medical student, general practitioner, pediatrician, internist, and resident in ophthalmology but also to the practicing ophthalmologist. The work is authoritative and reveals the skilled hands of Dr. Phillips Thygeson and Dr. Frederick Cordes, to whom the authors give much credit. The chapter on examination is well done and describes some of the more recent methods of diagnostic examination of the eye. Of particular value to the practicing physician is the chapter on the management of common ocular disorders. The sections on ocular emergencies in glaucoma are exceedingly important for the general practitioner. The authors stress the need for the cooperation of physicians in measuring intraocular tension during routine physical examinations in order that much of the unrecognized glaucoma may be diagnosed early and treatment instituted before irreversible ocular damage occurs.

Although there are no colored illustrations in the book, the black and white drawings and photographs are so excellent that except in the chapter on ocular disorder associated with systemic diseases the absence of color is unimportant. The chapter on trauma is brief but excellent and should be read by all who have to deal with ocular emergencies. It is especially recommended to the industrial surgeon. Chapter 13 (on neuro-ophthalmology) gives a brief but valuable outline of the subject which should be helpful to neurologists and neurosurgeons. The publishers have done a fine piece of work but ease and speed of reading might be facilitated if there were two columns to a page. This book is enthusiastically recommended to all who wish a clear, concise review of the essentials of ophthalmology.

Medical Department, United States Army: Preventive Medicine in World War II. Volume IV: Communicable Diseases Transmitted Chiefly Through Respiratory and Alimentary Tracts. Prepared and published under direction of Major General S. B. Hays, Surgeon General, United States Army. Editor in chief: Colonel John Boyd Coates Jr., MC. Editor for preventive medicine: Ebbe Curtis Hoff, Ph.D., M.D. Assistant editor: Phebe M. Hoff, M.A. Office of the Surgeon General, Department of the Army, Washington, D. C. Cloth. $5.50. Pp. 544, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1958.

This volume is a part of the clinical as distinguished from the administrative series on the history of the Medical Department of the Army in World War II. Two previous volumes on preventive medicine have been published. After an introductory chapter by Dr. John E. Gordon there are sections on diseases transmitted through the respiratory and alimentary tracts. Among others Dr. Joseph Stokes contributed chapters on chicken pox, mumps, measles, rubella, and pertussis; Dr. Philip Sartwell one on common respiratory diseases; Dr. Thomas Francis Jr. one on influenza; Dr. Joseph Smadel one on psittacosis; Col. L. A. Potter one on smallpox; Dr. A. C. McGuiness one on diphtheria; Dr. Esmond Long one on tuberculosis; Dr. Dwight Kuhns one on salmonelloses; Dr. Gail Dack one on food poisoning; and the late Gen. R. A. Kelser one on brucellosis. This partial list of contributors gives some idea of the high quality of the work. It is a great pity that we have had to wait so long for this volume and it hoped that the other volumes in this series will appear soon. The book has an index.

Rehabilitation Medicine: A Textbook on Physical Medicine and Rehabilitation. By Howard A. Rusk, M.D., Professor and Chairman of Department of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York, and 36 collaborators. With editorial assistance of Eugene J. Taylor, A.M. Cloth. $12. Pp. 572, with 172 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

Dr. Rusk and co-workers have attempted to cover a broad field within the confines of a relatively small book. They believe that the treatment of almost every type of illness, with the exception of minor injuries and simple acute infections, involves the process of rehabilitation. Part 1 deals with the principles of rehabilitation and part 2 with the application of these principles to specific disease problems. This book can be read with profit by the general practitioner or the specialist. Great emphasis has been placed on readability, and for this thanks is probably due Eugene J. Taylor, who is listed as an editorial assistant. The discussion of the principles of rehabilitation sums up everything the authors have talked and written about since the establishment of their service. It should provide an invaluable point of reference for these ideas, which are now collected for the first time under one cover. The fact that the emphasis on the activities of daily living as the focal point for rehabilitative therapy now seems so simple and familiar is almost entirely due to Dr. Rusk's persistence in forcefully supporting this concept.

The sections on electrodiagnosis and electrotherapy bring together many items formerly widely scattered. The chapter on writing prescriptions for rehabilitative treatment should be required reading for all physicians. The chapter on management of psychiatric problems is also excellent. It is hoped that in future editions the authors will eliminate the extended discussion of such an outmoded modality as ultraviolet ray therapy for the many conditions for which it is now recommended. In the discussion of the goniometer there is an apparently inadvertent omission of the method for determining the center of motion of a joint before attempting to measure the range of motion. The possible error is great when this point is neglected. The format of the book is conventional and attractive. There are many excellent photographs and useful charts.

Cyclopropane Anesthesia. By Benjamin Howard Robbins, B.A., M.S., M.D., Professor of Anesthesiology and Associate Professor of Pharmacology, Vanderbilt University School of Medicine, Nashville. Second edition. Cloth. $9. Pp. 293, with 74 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

This edition comes 18 years after the first. The author believes that this is the time for another unified discussion of the subject since there is an apparent increase in the use of cyclopropane in clinical anesthesiology in the United States. This monograph is a reference work and should not be considered a clinical textbook. Its bibliography is extensive, containing 353 references. After a description of the physical and chemical properties and listing the concentrations of cyclopropane needed for anesthesia and respiratory arrest, 110 pages are devoted to its effect on the circulatory system. This is the most extensive discussion in the book and reviews the literature at length. Other chapters discuss the effects of cyclopropane on the respiratory and gastrointestinal systems, the blood, and other tissues. The chapter on clinical administration includes descriptions of techniques that have been reported in the literature.

The author chose to include a short chapter on the relaxing agents because "the introduction of the relaxing agents in 1942 and the widespread use of one of them at the present time makes the use of cyclopropane even more satisfactory." He found no contraindications to the use of cyclopropane except where the explosion hazard (x-ray or cautery) is encountered and in circumstances where epinephrine will be used. The final chapter discusses the explosion hazard with cyclopropane. This monograph will be used by teachers and advanced students. It will not be of value to medical students or others with little clinical experience with cyclopropane. It is attractively composed and printed.

Chloromycetin (Chloramphenicol). By Theodore E. Woodward, M.D., and Charles L. Wisseman Jr., M.D. With collaboration of Harry M. Robinson Jr., M.D., and others. Foreword by Joseph E. Smadel, M.D. Antibiotics monographs no. 8. Under editorial direction of Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D. Cloth. $4. Pp. 159, with 19 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22. Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book is the eighth in a series of monographs published under the direction of the editors of Antibiotics Annual. The authors have produced a highly readable and selective review of the important studies that have been made concerning chloramphenicol, the first of the broad-spectrum antibiotics. There are chapters on the history, activity, properties, dosage forms and route of administration, side-effects, and the clinical results obtained in various infections. Pertinent information is included on the use of other antibiotics and drugs in chloramphenicol-susceptible infections. There is an extensive bibliography and a subject index. As a whole, this monograph should give most readers a balanced picture of the place which chloramphenicol has come to occupy in the treatment of microbial diseases. It should also be of particular value as a reference to and source of information about the drug.

Myasthenia Gravis. By Kermit E. Osserman, M.D., F.A.C.P., Physician-in-Charge, Myasthenia Gravis Clinic, Mount Sinai Hospital, New York. Cloth. $10. Pp. 286, with 58 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Queen St., Mayfair, London, W. 1, England, 1958.

A modern monograph on myasthenia gravis has been needed and is now provided by a physician who has had personal experience with more than 350 cases. Although not a common disease, it is being recognized with increasing frequency and, by its nature, it occupies a central position in the differential diagnosis of neurological disorders. With the decline of poliomyelitis it has become one of the most common causes of respiratory paralysis. The illustrations are clear and pertinent. A large number of references are given at the close of each chapter, and there is an adequate index. In this volume the author provides a comprehensive view of this disorder. Normal and abnormal functions of the neuromuscular junction, clinical features, diagnosis, and therapy by means of drugs and thymectomy all receive detailed attention. Much of the material has been published previously by the author but it is useful to have it collected in one volume. An excellent chapter on pathology is provided by Dr. Harvey Mendelow.

The author has performed a great service, but his conclusion must be accepted with some reservations because he is a therapeutic enthusiast. At the outset he states: "particularly in the last five years, new drugs and techniques of management have given the physician tools with which to make the myasthenic patient lead a more normal life." In discussing one of these new drugs, Mestinon, the author reports changes in the economic usefulness of his own patients and claims that "various clinics report up to 70 to 75 per cent increased clinical improvement (on Mestinon) as compared to Prostigmin," but examination of the reports cited does not bear out this contention. Many workers believe that the administration of the new drugs (Mestinon, Mytelase, or any of various experimental preparations) rarely makes a myasthenic patient significantly better than he was under therapy with neostigmine, which has been available since 1935. The value of the new drugs lies chiefly in the facts that their effects are more prolonged or the side-effects are less pronounced. The latter are usually evaluated according to the patient's statement rather than any objective criteria. The use of these drugs has not appreciably affected the mortality of the disease (15 to 30%), nor have they helped in establishing the indications for thymectomy. The author recommends the use of his edrophonium test to determine whether the patient is receiving adequate medication. This test has been widely accepted as a means of differentiating cholinergic from myasthenic crisis, although it has not yet been subjected to critical analysis or controlled study. Its value is not proved in the present monograph beyond the statement that "it is invaluable." Despite minor reservations of this nature, the monograph should be useful to the internists and neurologists who are responsible for the care of patients with myasthenia gravis.

Acetophenetidin: A Critical Bibliographic Review. By Paul K. Smith, Ph.D., Professor of Pharmacology, George Washington University School of Medicine, Washington, D. C. Monographs of Institute for Study of Analgesic and Sedative Drugs IV. Cloth. $5.75. Pp. 180, with 11 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book presents a critical review of the literature on the well-known analgesic-antipyretic agent acetophenetidin and its major metabolite N-acetyl-*p*-aminophenol (*p*-hydroxyacetanilid), to which the nonproprietary names acetaminophen and paracetamol have been applied. The book includes comments by the author as well as abstracts from the literature and from unpublished data. The main text covers the drug's history, chemistry, fate and metabolism in the body, antipyretic and analgesic actions, other therapeutic uses, effects on blood and other tissues, toxicology, tolerance, and habituation, and a summary. The bibliography and a general index appear at the end of the book. In addition to reviewing data pertaining only to acetophenetidin, the literature abstracted also includes studies of its comparative and/or combined action with such other drugs as aminopyrine, antipyrine, allylbarbituric acid, amobarbital, aspirin, salicylamide, and neocinchophen. This monograph should be of special interest and use to pharmacologists and clinical investigators as a critical guide to previously reported studies of the subject drug.

The Health of a Nation: Harvey W. Wiley and the *Fight for Pure Food*. By Oscar A. Anderson Jr Published with aid from Charles Phelps Taft Memorial Fund, University of Cincinnati. Cloth. $6. Pp. 333, with illustrations. Published for University of Cincinnati by University of Chicago Press, 5750 Ellis Ave., Chicago 37; Cambridge University Press, Bentley House, 200 Euston Rd., London, N.W. 1, England. University of Toronto Press, Toronto 5, Canada, 1958

This book deals with Harvey W. Wiley, M.D., who made a major contribution to the health of the United States. It should be of particular interest to students of the developments which led to the enactment of the laws which now serve to safeguard our food and drug supplies. The problems and controversies which confronted Dr. Wiley are ably presented. The author acknowledges the constructive part played by the American Medical Association and by individual physicians in the struggle to advance the public interest. Dr. Wiley, food adulteration, and claims for the alleged values of some medicines were and still are highly controversial topics. The book is a valuable contribution to an important field of public health history, even though some students may hold that the author's portrayal of Dr. Wiley's dynamic individualism is not all that he deserves.

The Recovery Room: A Symposium. By John Adriani, M.D., Professor of Surgery, School of Medicine, Tulane University, New Orleans, and John B. Parmley, M.D., Instructor in Surgery, School of Medicine, Tulane University. Publication number 340, American Lecture Series, monograph in American Lectures in Anesthesiology. Edited by John Adriani, M.D., Director, Department of Anesthesia, Charity Hospital, New Orleans. Cloth. $4.25. Pp. 123, with 17 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In this symposium on nursing and administration in anesthesiology the authors discuss, by means of questions and answers, the definitions, purpose, location, physical setup, administration, personnel, equipment, economics, policies and procedures, general patient management, and special problems of the subject. The illustrations are neat and easily read. This book should be available to nurses, interns, and residents in anesthesiology and surgery. It is neatly and simply organized and approaches the problem directly. Probably the greatest value of this book would be to those organizing a recovery room for the first time. Here they would quickly find the answer to most of their questions.

The Care of the Geriatric Patient. Edited by E. V. Cowdry, Ph.D., Sc.D., Director of Wernse Cancer Research Laboratory, Washington University School of Medicine, St. Louis. Cloth. $8. Pp. 438. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1958.

Care of the geriatric patient has become a prominent subject in the medical literature. This monograph begins with five lectures given to the Los Angeles County Medical Association in 1955, with the addition of discussions of various aspects of management of geriatric patients. Generally, it should serve as a reference book for anyone who treats elderly patients. This phase of patient care should be the function of all doctors and should not be classed as a specialty. This book is comprehensive and goes into various subjects thoroughly; indeed, it may embrace too much with regard to the various specialties. It is heartening to see included a discussion of care of the patient in his home because this aspect has heretofore been neglected. There is an excellent chapter on rehabilitation. Although the philosophy of the book is good, it is hoped that it will not make the reader think he has to be a specialist to care for elderly patients. This monograph should be added to the many books on this subject as a reference for the interested physician. One might wish that it were shorter, because it is doubtful that the busy physician will read it as thoroughly as he should.

Temporal Lobe Epilepsy: A Colloquium Sponsored by the National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda, Maryland, in Cooperation with the International League Against Epilepsy. Edited by Maitland Baldwin and Pearce Bailey. Co-editors: Cosimo Ajmone-Marsan, Igor Klatzo, and Donald Tower. Cloth. $15.50. Pp. 581, with illustrations and 1 chart in back pocket. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

It is not long since the temporal lobes, especially the right one, were counted among the more "silent" areas of the brain. Now they constitute one of the more fruitful fields for neurological investigation. Because they excite the interest of specialists in neurology, psychiatry, neurosurgery, anatomy, chemistry, endocrinology, pathology, electroencephalography, psychology, and other fields, there has sprung up in recent years a vast literature dealing with this portion of the brain. It is most valuable to have available authoritative summaries to which one not familiar with the field or without the time for fuller research may turn for information. This book is such a summary. It is a collection of the papers and the discussion presented at Bethesda, Md., in March, 1957. Those taking part in this symposium constituted most of the outstanding investigators in the world who have interested themselves in these problems. Their papers vary from extensive analyses of the material available to them to brief summaries of two or three pages. They represent many different viewpoints and opinions. The papers have been well prepared and are clear and concise. The discussion has been well edited without losing the spontaneity and often the sparkle which must have characterized this meeting. This is not an encyclopedia, but it is an excellent source of information for those who would bring themselves up to date on this subject and also a starting point for further, more detailed reading. The typography and format are good.

Radiology for Medical Students. By Fred Jenner Hodges, M.D., Professor and Chairman, Department of Radiology, University of Michigan, Ann Arbor, Isadore Lampe, M.D., Professor, Department of Radiology, University of Michigan, and John Floyd Holt, M.D., Professor, Department of Radiology, University of Michigan. Third edition. Cloth. $8.50. Pp. 450, with 109 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.

In this edition the authors have revised and reappraised certain portions and deleted others to make room for the inclusion of materials on new developments in diagnostic and therapeutic radiology. The book is intended for the undergraduate student of medicine. It presents basic principles and a fundamental understanding of radiology. The authors, using their book at Michigan to teach juniors, have dispensed with formal lectures, thus increasing the opportunity for informal teaching by means of the case method. The acceptance of this book is attested by the demand for this new edition. The first half is devoted to diagnostic radiology and includes well-chosen illustrations. A chapter dealing with the rapidly expanding field of cardiovascular radiology has been added; the section on pediatric radiology has been accorded proper attention; and material concerned with the biological hazards of radiation has been expanded. The remainder of the book dealing with therapeutic radiology has been revised, with the addition of new material concerning the use of radioactive cobalt (Co^{60}) and reflecting the declining use of radiation in the treatment of nonmalignant disease. In the final paragraph of the preface the authors express a hope that this new edition will serve as well as, if not better than, its predecessors. This book is recommended without reservation to medical students and their teachers. The postgraduate student in radiology should also find it useful, particularly if he is training in a teaching hospital.

Polarography in Medicine, Biochemistry, and Pharmacy. By M. Brezina and P. Zuman. With foreword by J. Heyrovsky. Translated from Czech by S. Wawzonek. [English edition revised from second Czech edition.] Cloth. $19.50. Pp. 862, with 319 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88/90 Chancery Lane, London, W. C. 2, England, 1958.

In this thoroughly annotated bibliography of the literature of polarographic analysis in the fields of medicine, biochemistry, and pharmacy through 1954, theoretical considerations are touched on only briefly as are descriptions and discussions of general instrumentation. The book is intended mainly to serve the practicing analyst as a survey of the published methods and as a laboratory reference text. Most of the methods are given in sufficient detail for the experienced analyst to use without referring to the original work. About half of the references are to non-English language publications. The text is divided into sections covering the analysis of inorganic compounds, including elements and anionic groups, as determined in air, water, soil, drugs, and in plant and animal tissue. Organic compounds are classified by chemical functional group and also as biochemical classes in which are included vitamins, hormones, alkaloids, and miscellaneous steroids. Proteins and enzymes are treated separately. Tables of important buffers and of half-wave potentials are included. The book should be of great value to those engaged in the analysis of materials of biochemical interest who use the polarographic technique.

Muir's Text-Book of Pathology. Revised by D. F. Cappell, C.B.E., M.D., F.R.F.P.S., Professor of Pathology, University of Glasgow, Glasgow, Scotland. Seventh edition. Cloth. $14.50. Pp. 1201, with 733 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1958.

This new edition of a well-known text is intended primarily to meet the requirements of undergraduate medical students. Accordingly, it follows the established pattern of such textbooks. Disturbances of the circulation; inflammation; nonspecific and specific granulomas; repair and hypertrophy; disturbances of nutrition; retrogressive changes; infection, fever, and immunity; tumors; and etiological factors in tumor growth are discussed in that order. The latter chapters are devoted to special pathology of the body systems. The text is written in a lucid style. In the course of revision the author has rearranged it to incorporate new material. He emphasizes the importance of the autopsy in the teaching of pathology and the absolute necessity for experience gained through this discipline. There is a list of references. This textbook on general and special pathology meets fully the needs of the undergraduate medical student and also serves as an excellent reference source for pathologists in practice.

QUESTIONS AND ANSWERS

REHABILITATION AFTER A HEART ATTACK

To the Editor:—*A 46-year-old patient sustained a mild myocardial infarct. He had pain in the posterior chest wall but did not seek medical aid until a month later, when angina on effort became more pronounced and he complained of "skipped beats" (pulsus bigeminus and pulsus trigeminus). He was hospitalized, maintained on bed rest and quinidine therapy, and discharged after six weeks. He convalesced at home for six more weeks and now has a vocational problem. He has been offered a position 400 miles from his home. This would involve moving his family and reestablishing his home elsewhere early in 1959. He would be required to be available for night work once every two weeks. Would such a change for this patient be considered hazardous?*

M.D., Ohio.

Answer.—This patient presents a problem in rehabilitation. Initially, a month passed before he saw his physician; then he had six weeks of rest at the hospital and six additional weeks at home. He therefore has had about four months of convalescence since his original myocardial infarct. This is a sufficient period for maximum healing. Factors that would limit his activity would be increased heart size, high blood pressure, and exertional dyspnea and angina. Assuming that he has none of these, there should be no reason why he is not physically capable of taking on a new position. The required moving of his family, reestablishment of his home, and occasional night work would have no particular harmful effects. The decision must be based, in large part, on socioeconomic factors, and these are not stated. If a man has experienced a myocardial infarction and has made a fairly satisfactory recovery, there is no reason to treat him as if he were fragile. In terms of his survival, proper diet, proper weight, and adequate activity are far more valuable than oversolicitous medical conservatism.

INHALATION OF PURE OXYGEN

To the Editor:—*How long may man breathe 100% oxygen without injurious effect?*

M.D., California.

Answer.—There now exists a sizable body of information about oxygen intoxication, some of it relating to retrolental fibroplasia and other effects on infants and some relating to the effects of oxygen inhaled under pressures higher than one atmosphere by divers. A normal man can breathe pure oxygen at atmospheric pressure continuously for 14 to 24 hours before developing a mild pulmonary irritation, according to Lambertsen (Respiratory and Circulatory Actions of High Oxygen Pressure, in Proceedings of the Underwater Physiology Symposium, Publication 377, Washington, D. C., National Academy of Sciences–National Research Council, 1955, page 25). Infants are more susceptible to oxygen intoxication, and, according to Everett (*A. M. A. Arch. Ophth.* 56:481, 1956), for all practical purposes there is no concentration of oxygen in excess of that in air that is not associated with risk of developing retrolental fibroplasia. Prolonged action of oxygen in sufficient concentration causes vasoconstriction within the brain and inhibits certain enzyme systems, in addition to the local effects on pulmonary epithelium. In mice, a striking effect on length of life is seen at a critical concentration of oxygen near 70%. Living continually in atmospheres of 20 to 70% of oxygen has little effect on the length of life of the laboratory mouse, but Gerschman and co-workers (*Am. J. Physiol.* 192:563, 1958) found that at concentrations between 70 and 100% there is a critical point that cannot be exceeded without markedly shortening the life of the mouse.

SENSITIVITY TO LIGHT

To the Editor:—*Several years ago when sun lamps were popular, a man now in his 60's used his sun lamp quite often with the result that he not only has what resembles an x-ray burn but also has become sensitive to sunlight and even fluorescent light and television light under certain conditions. Even his office is free from sunshine. All medical evaluation otherwise gives negative results. His main complaint after exposure is that he "feels awful" and "all in." Can any preparation be used to protect him?*

M.D., New York.

Answer.—Interpretation of this problem necessitates a complex answer. If sunshine causes the patient to "feel awful," he may be suffering from porphyria of the intermittent-acute or chronic-mixed form. His urine should be examined during an acute attack for the presence of a port-wine color, coproporphyrin, uroporphyrin, porphobilin, and porphobilinogen. If porphyria is present, the ingestion of alcohol should be avoided. Also, under these circumstances the functions of the liver should

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

be investigated by appropriate tests. If the skin shows changes which are equivalent to a chronic radiodermatitis (atrophy, telangiectasia, hyperpigmentation, hypopigmentation, ulceration, keratoses, and epitheliomas), the therapeutic and prophylactic problem is different. In the latter case, the keratoses and epitheliomas should be removed, preferably by surgical excision, as dictated by clinical necessity. Surgical planing would improve the texture and appearance of the skin and would decrease the future formation of malignant and premalignant cutaneous neoplasms. Sun screens may assist in preventing further degeneration of the skin, especially after dermabrasion. An antimalarial preparation (250 to 500 mg. of chloroquine one to four times a day by mouth) may decrease photosensitization. Avoidance of sunshine, as far as is practical, should be practiced. Mechanical protection, such as the wearing of a hat and long sleeves, is to be recommended even during overcast weather. Sunbathing and exposure to reinforced solar radiation near bodies of water is contraindicated.

TRANSFUSIONS FOR PATIENTS WITH CANCER

To the Editor:—*This question relates to giving blood to patients entering the hospital in terminal or near terminal stages of carcinomatosis. These patients are not suffering any blood loss from acute gastrointestinal, pulmonary, or uterine hemorrhage. For example, a 52-year-old woman was admitted to the hospital with multiple osseous metastases. Four years previously she had a radical breast amputation for carcinoma. She had x-ray therapy after this operation. During a 14 weeks' stay in the hospital, she received 6 pints of blood. In another instance, a 77-year-old man was admitted to the hospital with severe anemia from carcinoma of the stomach. He received 5 units of blood but died 11 days after admission. Another man, aged 73, was admitted with carcinoma of the colon with metastases; he also had diabetes and hypertensive heart disease. He received 4 units of blood but died eight days after admission. Are blood transfusions indicated in such patients?*

M.D., Illinois.

Answer.—In this setting transfusions are considered as symptomatic or palliative treatment. Therefore, if the patient has symptoms reasonably attributable to anemia per se and if the anemia cannot be corrected by some other means, transfusions are indicated regardless of the patient's poor prognosis. Since the degree of anemia which will produce symptoms depends on the patient's activity and a number of other factors, the evaluation of the need for transfusion should be based on bedside observation rather than any arbitrary hemoglobin value. Patients with anemia due to disseminated cancer, not complicated by blood loss, characteristically have only a moderate anemia which is usually asymptomatic, particularly in those patients whose activity is limited. Most such patients, therefore, are not perceptibly benefited by transfusion. From these statements, it may be seen that the question of whether transfusion therapy was indicated in the cases cited cannot properly be evaluated without knowing more details of these patients' symptoms. It should be emphasized, however, that patients with incurable cancer deserve as careful and considerate symptomatic or palliative treatment as patients ill with non-neoplastic diseases.

LENSES FOR RETINITIS PIGMENTOSA

To the Editor:—*Will any type of lens allow vision from various parts of the retina in patients with retinitis pigmentosa?*

O. C. Amstutz, M.D., Irvine, Ky.

Answer.—There are no lenses especially designed or particularly adaptable for patients with retinitis pigmentosa. Lens systems are designed for eyes that have unusual optical disorders that cannot be corrected by single-piece lenses such as are worn in the usual spectacle frame. The result is an enlarged image on the retina that is helpful in patients with central retinal defects in providing vision in ordinary light. In persons with retinitis pigmentosa, central vision usually remains after peripheral areas of the retina become insensitive to light; consequently, an enlarged image does not materially improve vision. Colored lenses are helpful only in reducing glare or protecting the diseased and impoverished retinal elements from excessive light. The qualified answer to the question is "no."

FEATHERS AND SCALES

To the Editor:—*Prof. P. E. Raymond (Prehistoric Life, Cambridge, Mass., Harvard University Press, 1939, p. 184) has stated: "The scales in fish and the feathers in birds arise from different layers of the skin." Is this correct?*

John R. Howitt, M.D.
Port Arthur, Ontario, Canada.

Answer.—Professor Raymond's statement is correct. Earlier descriptions in comparative anatomy often created artificial series of analogous rather than homologous structures. Fish scales, whether of shark, sturgeon, or trout (placoid, ganoid, or cycloid types of scales, respectively) are derivatives of the dermis. The epidermis of fishes is very thin and never cornifies, and the scales remain embedded in the dermis. In sharks the teeth are modified scales. During the development of a feather there is a transitory dermal papilla which degenerates into the nonliving pulp. Barb and barbules originate entirely from epidermal cell columns which cornify. A feather, therefore, represents a complex modification of the epidermis. The presence of a dermal papilla during the development of fish scales and of feathers probably led to the mistaken identification of such structures. Even a down feather is not an "elongated and frayed out scale."

Scales of reptiles and those on the legs of birds, however, are of epidermal origin. In these animals they represent a thickened stratum corneum and more nearly resemble feathers than do the scales of fishes.

INDURATED SCAR

To THE EDITOR:—*About six weeks ago, a 14-year-old boy received a minor bruise in his upper lip. There was some exudation and slight bleeding at the time, but in a week all external evidence of the injury disappeared. There is, however, a definite area of scar tissue, flat and pea-sized in diameter, that has persisted in size and consistency. There is no possibility of foreign body. A similar scar was removed recently from another patient in the belief that it was a foreign body, but it recurred two weeks later. The scar tissue is not painful, but the boy is a capable cornetist and his teacher has advised him not to play his instrument or any other instrument involving the use of the lips until all evidence of this injury disappears. Is there anything that might speed his recovery?*

Louis H. Bos, M.D., Rehoboth, N. Mex.

ANSWER.—From the description given there was no evidence of a break in the skin of the upper lip. If there was such a break, the wound has apparently healed by secondary intention, leaving a scar both on the skin surface and in the subcutaneous tissue. It is not uncommon for such a scar to continue to be felt for three to six months after all external evidence of injury has disappeared. Some people are more subject to hypertrophic scarring than others. The softening of the scar might be hastened in its early stages by gentle massage with some such substance as cold cream or cocoa butter. It is questionable whether such a procedure would be of any value at this late stage, but the scar should become soft in time, permitting the boy to return to his cornet playing.

CORAL POISONING

To THE EDITOR:—*What is the cause and treatment of "coral poisoning" (infected abrasions from coral)?* *D. D. Dieter, M.D., Eustis, Fla.*

ANSWER.—Coral cuts are generally the result of brushing against or carelessly handling the sharp exoskeletons of various species of stony corals—members of the Coelenterata, order Anthozoa. The severity of the lesion depends on such factors as degree of laceration of the skin, introduction of foreign substances into the wound, venom from the stinging tentacles of the coral polyp, and secondary bacterial infection. Treatment consists of prompt cleansing of the wound, removal of foreign particles, débridement if necessary, and application of antiseptic agents. In severe cases it may be necessary to give the patient bed rest with elevation of the limb, kaolin poultices, dressings of magnesium sulfate in glycerin solution, and antibiotics. A detailed discussion of coral cuts is given by Halsted (Dangerous Marine Animals, Cambridge, Md., Cornell Maritime Press, 1958).

TRACHEAL SCLEROMA

To THE EDITOR:—*What is the latest treatment for scleroma of the subglottic area of the trachea?*

Phelps P. Luria, M.D., Far Rockaway, N. Y.

ANSWER.—Scleroma is a chronic granulomatous disease which may affect any part of the respiratory tract. The diagnosis is based on cultures and biopsy specimens revealing the Fritsch bacillus (Klebsiella rhinoscleromatis), Russell's bodies (nonspecific eosinophilic masses thought to represent degenerated plasma cells), and the characteristic Mikulicz's cells (foamy abundant pale cytoplasm with a relatively small nucleus). Subglottic infiltration in scleroma may cause respiratory obstruction. Tracheostomy may be necessary if removal of the offending tissue does not alleviate respiratory embarrassment. In the active phase of the disease, treatment with tetracyclines or streptomycin is the current method of choice and represents a notable improvement over previous symptomatic measures. Cessation of activity in scleroma is often followed by scarring and stenosis of the larynx or upper trachea. Under these circumstances it is feasible to restore the lumen by removal of scar tissue and to insert a skin graft which can be maintained in position by some type of mold until healing has taken place.

SMALLPOX VACCINATION AND TUBERCULOSIS

To THE EDITOR:—*Please give information on the effect of smallpox vaccination on undiagnosed primary tuberculosis of infancy.*

E. P. Dale, M.D., Los Angeles.

ANSWER.—There seems to be no valid contraindication to smallpox vaccination in undiagnosed (or diagnosed) primary tuberculosis in infancy. If there were a concealed risk in this situation it should have been well demonstrated by experience. It was formerly the custom in many communicable disease hospitals to vaccinate all patients on admission. In countries where both smallpox and tuberculosis are prevalent, smallpox vaccination is currently performed without reference to preexisting tuberculosis. In neither situation is there any evidence that vaccinia accelerates the tuberculous process. In the United States, under current conditions the time of vaccination is an elective matter and the infant should be vaccinated when he is in normal health, but there is no reason to fear the existence of undiscovered primary tuberculosis.

TESTS FOR SPINAL FLUID LOSS

To THE EDITOR:—*Please give a list of tests and references for the identification of spinal fluid escaping through basal skull fractures and the nose. Also, please outline the advantages and disadvantages of spinal injections of methylene blue as a test for such a fracture.*

Joseph Catton, M.D., San Francisco.

ANSWER.—Grossly, especially when the patient leans forward, a clear, odorless fluid in quantity may be collected in a test tube. No sediment is evident on standing. The specific gravity is between 1.005 and 1.010. The normal sugar content of the cerebrospinal fluid of fasting persons is between 50 and 80 mg.%. It is necessary only to demonstrate the reduction of copper sulfate in the collected fluid. The collected fluid will contain no mucin or albumin and only an occasional lymphocyte. It is possible to demonstrate the location of a fracture in the cribriform plate by the injection of 3 to 5 cc. of a 0.6% solution of indigo carmine into the spinal canal. A bluish green fluid will make its appearance in the nasal discharge within 10 to 15 minutes.

ALLERGY TO PENICILLINASE

To THE EDITOR:—*A question and answer on allergy to penicillinase appeared in* THE JOURNAL, *Dec. 20, 1958, page 2207. I initiated the original in vivo and clinical studies pertaining to the use of penicillinase in the treatment of penicillin reactions. It is true, since penicillinase is a protein, that allergic reactions may occur after repeated injections of the enzyme, but when repeated injections are needed they are given over a short period during treatment of the penicillin reaction and there would not be time enough for antibodies to develop which would produce an immediate allergic reaction. If a patient received a further injection or injections of the enzyme months later, then a true allergic reaction might become manifest. The reactions to penicillinase referred to in the answer (including fever and chills), which has been described by me as well as by Zimmerman, cannot be classified as allergic. To my knowledge, about six such reactions occurred in about 300 treated patients. This represents more of a Herxheimer type of reaction, but it is still a mysterious entity.*

Regarding the time factor in using penicillinase in immediate reactions to penicillin, it may be said that within 15 minutes after an intramuscular injection of penicillinase no circulating penicillin can be detected and this would hold even for a shorter period if the enzyme is injected intravenously. If a patient dies within a minute or so after receiving penicillin one would mechanically be unable to get the enzyme into the patient in time, but in many immediate reactions patients go into shock and may be maintained with epinephrine and pressure substances for many hours. In this situation penicillinase can be lifesaving by immediately destroying the offending antigen. Concerning the last sentence, that penicillinase "may be of value in delayed reactions," it can be said that it has proved to be of great value in delayed reactions. In many patients the results have been nothing short of dramatic. In two patients with complete anuria for days associated with a penicillin reaction with no response to conventional means of treatment, marked diuresis began as soon as four hours after the injection of penicillinase.

Robert M. Becker, M.D.
3414 Monroe St.
Madison, Wis.

The above comment was referred to the consultant who answered the original question, and his reply follows.—ED.

To THE EDITOR:—*Nothing in the original reply contradicts the correspondent's statement that allergic reactions to penicillinase might develop primarily after repeated injections, and nothing was said to contradict the opinion that the febrile reactions are not allergic. The acute anaphylactic symptoms produced by penicillin are produced by the sudden release of excessive amounts of histamine or other mediators responsible for the shock symptoms. This is the result of antigen-antibody union. After such a release one could presumably destroy all remaining penicillin and yet not prevent a fatal outcome, because the mediators already released are responsible for the shock. The major problem there is to counteract the effect of these mediators (such as with vasodilatation and bronchial constriction) and later to give medication to make the mediators, particularly histamine, inactive by administering antihistamine. This consultant has no objection to the use of penicillinase as long as the physician does not get the impression that it is the first line of procedure in combating anaphylaxis. Epinephrine, aminophylline, and antihistamine, in that order, are far more important. The correspondent takes issue with the use of the term "may." Does he claim that it is of value in all patients with delayed penicillin reactions? If so, both the published reports and my own experience contradict that contention. The fact remains that penicillinase may or may not be of value in treating delayed reactions.*

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LIFE-TABLE ANALYSIS OF SURVIVAL AFTER CEREBRAL THROMBOSIS—TEN-YEAR EXPERIENCE

Roger W. Robinson, M.D., William D. Cohen, Ph.D., Norio Higano, M.D., Richard Meyer, M.D.
Gerhard H. Lukowsky, M.D., Robert B. McLaughlin, M.D.
and
Harold H. MacGilpin Jr., M.D., Worcester, Mass.

Factors of possible prognostic value have been sought in the records of 1,018 patients with cerebral thrombosis admitted to three major hospitals of Worcester during the years 1947 through 1956. The initial attack was fatal in 21% of the cases. Of the 737 patients who survived the first episode of thrombosis, 50% died within 4.1 years, while only 18% of a comparable sample of the general population died within that time. The principal cause of subsequent mortality was recurrent vascular disease, which accounted for 85% of all deaths. There were no important differences between those who survived and those who did not survive the first attack in regard to the incidence of coronary disease, diabetes mellitus, and hypertension, but the association of congestive heart failure with cerebral thrombosis was found to carry a poorer immediate prognosis. Additional factors adversely affecting prognosis were severe initial attacks, and early recurrences.

THE INCREASING prevalence of cerebral thrombosis in the United States has created many medical, social and economic problems.[1] General pessimism by many in the medical profession toward patients with this disease has retarded interest in any systematic study of its natural course or therapy to improve the status of patients so afflicted. The present investigation of cerebral thrombosis, with use of life-table analysis, was undertaken to determine the factors influencing survival of patients after an initial episode and to aid in designing experimental therapeutic programs. An adequate study of the life history of patients with this disease requires a highly stable population of adequate size that is traceable to determine survival rates. Worcester, Mass., with a metropolitan population of over 500,000, meets these requirements. It was therefore possible to complete such a study.

Material and Methods

A record review of all patients with a diagnosis of cerebrovascular disease admitted to the Memorial, St. Vincent, and Worcester City hospitals during the years 1947 through 1956 was made. Patients with intracranial and subarachnoid hemorrhage,

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From the Research Laboratory and Medical Division, The Memorial Hospital, and medical divisions, St. Vincent and Worcester City hospitals.
Read, in part, before the Third World Congress of Cardiology, Brussels, Sept. 17, 1958. Read before the New England Cardiovascular Society, Boston, Jan. 12, 1959.

embolism, and neoplasm were excluded. The clinical criteria used to confirm the diagnosis of cerebral thrombosis were those outlined by the *ad hoc* committee of the National Institute of Neurological Diseases and Blindness, under the chairmanship of Dr. Clark H. Millikan.[2] One thousand eighteen records of patients with definite cerebral thrombosis were available for analysis. Of the patients surviving the studied admission, more than 97% were traced by a public health nurse employed by the Research Laboratory. Survival data and appropriate information from the records were transferred to check-cards for sorting. Facts regarding mortality, survival, recurrence, and severity of initial attack were organized in life-table form, as described by Hill.[3] Deaths from all causes were included, and a few patients lost sight of prior to 1957 were included in those exposed to risk for the recorded years only. For comparison, life-tables were constructed based on the New England white population from the United States Census of 1950,[4] adjusted for age and sex. Patients whose initial episodes of cerebral thrombosis occurred prior to 1947 were excluded. The severity of the initial attacks of the remaining survivors was graded as follows: grade 1—few neurological signs and symptoms without residual disability (grade 1A, minimal signs and symptoms, e. g., monoparesis, monoplegia, aphasia, or cranial nerve signs, and, grade 1B, transitory hemiparesis or hemiplegia); grade 2—some neurological signs and symptoms with minimal residuals; grade 3—gross neurological signs and symptoms with disabling residuals; and grade 4—total, permanent incapacitation and/or death due to cerebral thrombosis.

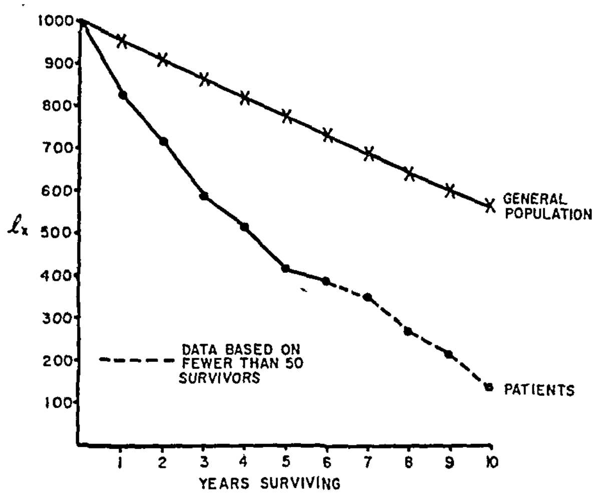

Fig. 1.—Survival of patients with cerebral thrombosis compared to New England population of same age and sex distribution.

Results

Mortality.—A comparison of the mortality among the survivors of an initial attack of cerebral thrombosis with that expected in the New England white population of similar age and sex is shown in figure 1. The abscissa represents years of survival after the first episode and the ordinate (l_x) the number remaining alive at each year, adjusted to 1,000 initial survivors. During the studied admission 196 patients died, an initial mortality of 21%. The lower curve in the figure was derived from records of 737 patients, the 79% who survived the initial attack. It is clear that, within one year, more than 15% of these survivors had died, in contrast to about 5% in the curve drawn for the hypothetical comparable New England population. Fifty per cent of the patients were dead within 4.1 years, while at the same time only 18% of the general population would have died. The five-year mortality of 59%, in contrast to an expected mortality of 23%, shows that these patients are dying about two and one-half times faster than the general population. Beyond the sixth year the data are unreliable, since the calculations had to be based on fewer than 50 survivors. These results are similar to those recently reported by Pincock,[5] but his survival rates were somewhat higher. As this author points out, however, his results cannot be compared with those of patients from an unselected general hospital population because of the all-male veteran character of his group. Also, there were only 101 survivors available for his follow-up study. Another recent report by Pierson and Hoobler[6] showed mortalities of 10 to 15% per year, comparable to those of the present study. However, the selection of hypertensive sub-

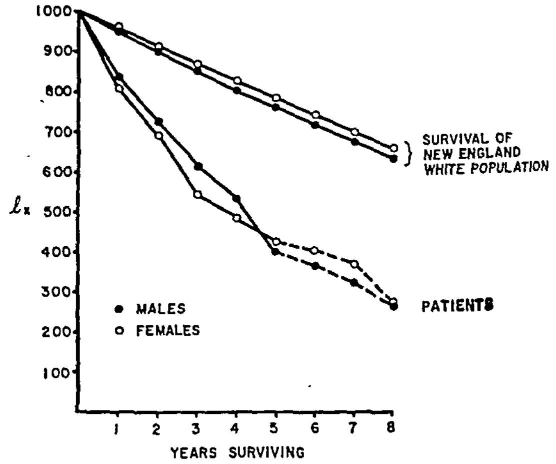

Fig. 2.—Survival of men and women with cerebral thrombosis compared to New England population of same age distribution.

jects under the age of 50 with a previous episode of "focal encephalopathy" restricted this study to an analysis of 71 patients.

Survival.–The similarity of survival rates in men and women is shown in figure 2. The apparent greater survival at three years of men over women does not reach statistical significance, the probability of chance occurrence (p) being about 0.08 by the chi-square test.[7] The average ages of the men (66.2 years) and women (68.0 years) were similar. Although the increased survival rate of women over men in the New England population does not seem great in this figure, these differences are highly significant because of the large size of the studied population.

Despite the similar survival rates of the men and women, a larger number of women were found in the 196 patients who succumbed during the initial episode of the disease. Indeed, of these patients only 36% were males, representing 17% of all males studied, while the 64% of the 196 who were females represented 25% of the women in the entire group. In an attempt to determine the reasons for this greater mortality in women, several pertinent complicating factors were studied, as shown in table 1. Since any sex differences in age and complications were found to be insignificant, the explanation for the difference in mortality remains obscure. This table also reveals that survivors of an initial cerebral thrombosis had a much lower incidence of congestive heart failure (18%) than did those who died (33%)–($p<0.001$). Thus, the association of congestive heart failure with cerebral thrombosis carries a poorer immediate prognosis. There were no important differences in the incidence of coronary disease, diabetes mellitus, and hypertension between those succumbing to and those surviving the initial episode.

TABLE 1.–*Incidence of Complications in Men and Women Who Died at First Attack Compared to Incidence Among Survivors*

	Died at First Attack		
	Males	Females	All Survivors
Patients, no.	66	116	535
Mean age, yr.	69.6	73.6	68.1
Complication			
Coronary disease, %	20	16	21
Diabetes, %	18	17	13
Hypertension, %	68	69	70
Congestive heart failure, %	32	31	18
None, %	17	10	19

Of the 737 patients who survived the initial attack, 344 have since died. The causes of death were ascertained from hospital records (some of which included autopsy reports), death certificates, and, in a few instances, interview of relatives. In table 2 are listed both vascular and miscellaneous causes of death in both males and females. As anticipated, recurrent cerebral vascular disease accounted for 53% of all deaths. This is comparable to the 60% reported by Pierson and Hoobler[8] in their series of 71 patients. An additional 29% of the deaths in the present series were due to coronary disease, with a total of 85% resulting from all vascular causes.

TABLE 2.–*Causes of Death in Survivors of First Attack of Cerebral Thrombosis*

	Male (166 Patients)		Female (178 Patients)	
	No.	%	No.	%
Cerebral	87	52	97	54
Coronary heart disease	46	28	53	30
Renal	4	3	2	2
Peripheral vascular disease	1		1	
Total cardiovascular-renal	138	83	153	86
Miscellaneous	28	17	25	14
Bronchopneumonia	14		10	
Cancer	6		7	
Other	8		8	

Recurrence.–In order to study the relationship between early recurrence of cerebral thrombosis and increased mortality, 535 survivors, all those for whom such information was available, were divided into those with recurrence within two years of the initial episode and those without recurrence during this interval. Since at least a two-year follow-up study was necessary, only patients whose first experience occurred between 1947 and 1955 were included. The two groups were similar in size, age, and incidence of complications, as shown in table 3. The higher incidence of congestive heart failure in the early recurrence group was not statistically significant ($0.05<p<0.10$). But life-table analysis of these patients, shown in figure 3, clearly demonstrates that those with early recurrences had a much higher mortality, with a 50% survival of only two and one-half years, compared with nearly seven years in the group without early recurrence. Thus, these studies provide statistical evidence for the clinical impression that early recurrence is correlated with poor survival. A more detailed analysis of cumulative recurrences after the initial attack

TABLE 3.–*Similarity of Incidence of Complications in Patients With and Without Early Recurrence*

	Recurrence		
	Within 2 Yr.	None Within 2 Yr.	All Survivors
Patients, no.	225	310	535
Mean age, yr.	68.8	67.5	68.1
Complication			
Coronary disease, %	22	19	21
Diabetes, %	13	13	13
Hypertension, %	72	69	70
Congestive heart failure, %	22	16	18
None, %	17	20	19

revealed that over one-third of the patients suffered a recurrence within one year, one-half within two years, and two-thirds by the end of the fourth year.

Severity of Initial Attack.—In order to evaluate the relationship between severity of the initial attack of cerebral thrombosis and mortality, 642 survivors for whom there was sufficient information to grade severity were analyzed by means of life-tables. The tables for grades 2, 3, and 4, all those with residual disability, were combined, since there was no appreciable difference in mortality among them. In figure 4 this combined group is compared with the survivors in grade 1, those without residuals. At three years, the difference in mortality favoring the less severe group (grade 1) was highly significant ($p<0.001$). Since this figure illustrates the difference in mortality between those without and those with residual signs and symptoms, it was of interest to subdivide further the grade-1 group into those with minimal signs and symptoms, grade 1-A, and those with transitory hemiparesis or hemiplegia, grade 1-B. A comparison of the three-year survival rate reveals that group 1-A had only slightly greater mortality than the general population (811 compared with 864 still alive), whereas group 1-B had a mortality nearly comparable to groups 2, 3, and 4 (608 compared with 561 still alive). Thus, despite complete recovery without residual disability, those whose first episodes were more severe and extensive had a much less favorable prognosis than the patients experiencing only mild initial attacks.

Summary

An initial attack of cerebral thrombosis was accompanied by a mortality of 21% in an unselected group of over 1,000 patients admitted to the three major hospitals of Worcester, Mass. Of the 79% surviving the first episode, half had died within 4.1 years, in contrast to an expected mortality of only 18% during this time in the general population, adjusted for age and sex. Although the mortality in women was higher during the initial attack, no sex difference was apparent in long-term survival.

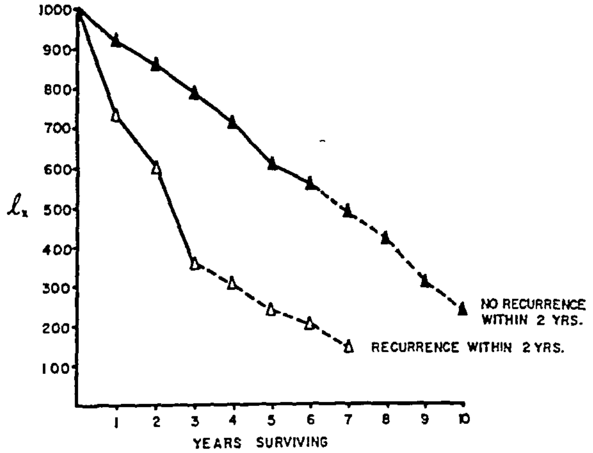

Fig. 3.—Difference in survival of patients with and without early recurrence.

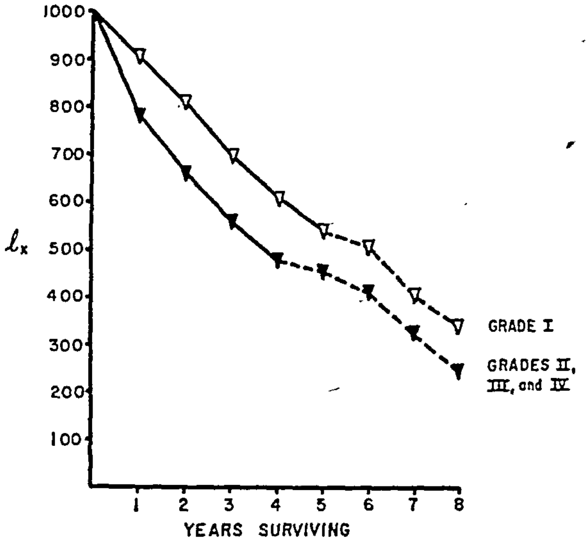

Fig. 4.—Influence of residual disability on survival in cerebral thrombosis.

The principal causes of death in patients surviving the initial attack were recurrent cerebrovascular disease and other vascular disorders, accounting for 85% of all deaths. The three factors that adversely affected prognosis were associated congestive heart failure, more severe initial attacks, and early recurrence of the disease.

119 Belmont St. (5) (Dr. Robinson).

This study was supported by a grant from the Albert and Mary Lasker Foundation.

Statistical advice in this study was supplied by Dr. Jane Worcester, Department of Biostatistics, Harvard School of Public Health.

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TUBE FEEDING

Willard A. Krehl, M.D., Ph.D., New Haven, Conn.

Two types of pabulum for administration by nasogastric tube were studied in nine patients who were unable to swallow. Pabulum no. 1 was made from powdered skimmed cow's milk with the addition of cream, glucose, strained liver, and a vitamin concentrate. Pabulum no. 2 was made by a simple formula from one 15.5-(fluid) oz. (458 cc.) can of commercially available soy bean milk diluted with an equal volume of water and supplemented with the same vitamin concentrate. After a week or more on formula no. 1, all patients had diarrhea. After changing to formula no. 2, five became free of diarrhea within 36 hours. Two of the nine patients did not do well on either formula. Analyses of blood, made in all patients at the beginning and end of a two-week period on formula no. 2, showed no indications of biochemical upsets, and there was no clinical evidence of malnutrition. This simple preparation for tube feeding was tolerated by most patients for at least two weeks with a minimum of gastrointestinal and biochemical complications.

In patients to whom intravenously given fluids can no longer supply adequate nutrition, especially calories and amino acids, tube feeding is often used. Material for tube feeding is formulated so as to provide an adequate level of all nutrients within the range of recommended dietary allowances. Aside from supplying adequate nutrition, tube feeding formulas should fulfill the following criteria: (1) be well tolerated and not induce vomiting; (2) be of proper fluid consistency so as to be easily administered and to supply a sufficient water intake; (3) produce a minimum of gastrointestinal complications, such as excessive flatulence, constipation, abdominal distention, and diarrhea; (4) be easily prepared from readily available and reasonably inexpensive materials; and (5) be homogeneous in composition. Palatability of the tube feeding formula, while not of prime importance, is certainly desirable.

The principal tube feeding formula used in the Grace–New Haven Community Hospital is nutritious and generally satisfactory. However, it does require special preparation by the dietetics department, and in a considerable number of patients it produces soft, loose stools and even frank diarrhea. In an attempt to find a tube feeding formula which might produce fewer gastrointestinal complications, such as diarrhea, and be more easily and quickly prepared on the ward, canned soy bean milk[1] was used in 12 selected patients who had first received the usual tube feeding formula no. 1 (analyzed in table 1).

That soy bean milk might be well suited for tube feeding is evident from the ample support in the literature for its use in the management of conditions involving the gastrointestinal tract, such as peptic ulcer, and as a hypoallergenic food for infants, children, and adults. Balfour[2] has noted that foods used in the treatment of upper gastrointestinal irritation should be easy to digest, should contribute little roughage, and are most effective when given in small, frequent feedings. He has observed further that soy bean milk has been noticeably more soothing than ordinary milk to the upper gastrointestinal tract and is seemingly easier to digest. Burke and co-workers[3] found that soy bean milk is as effective as the Sippy milk and cream regimen insofar as influencing the concentration of gastric acidity is concerned.

Glaser, who has studied the problem of allergy in infants, has had wide experience in the use of soy bean milk as a hypoallergenic food. He has reported[4] the successful use of soy bean milk in over 85% of cases in feeding infants from birth and that this may later be substituted by cow's milk formulas without difficulty, except in those infants in whom there is probably a persistent congenital sensitivity to cow's milk.

Procedure

Nine patients were used in this study, four men and five women, with an over-all age range of 55 to 94 years. Eight of the patients were hospitalized because of severe cerebral vascular accidents, while one patient had postencephalitic paralysis agitans (Parkinson's disease). The latter patient was comatose, was unable to move any extremity, and could not swallow. The other eight patients had hemiplegia and were unable to swallow readily without aspiration. Lumbar punctures were done on all the patients, but only two had red blood cells in the cerebrospinal fluid in sufficient number to indicate bleeding associated with the cerebral vascular accident. None of the patients received anticoagulation therapy. On admission to the hospital, the patients were all given fluids intravenously for periods rang-

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Associate Professor of Nutrition, Nutrition Laboratory, Yale University School of Medicine.

ing from three days to one week, and attempts were made routinely to establish whether they could swallow water without aspiration. When it had been established that the patients could not swallow sufficiently well to provide adequate nutrition, the intravenous therapy was discontinued and a nasogastric tube was passed in preparation for tube feeding. Two types of nasogastric tubes were used, i. e., a soft rubber Glenn tube and a small plastic Levin tube. The former tube is preferred because its soft, collapsible, pliable structure minimizes esophageal irritation.

TABLE 1.—*Analysis of Gastrostomy Tube Feeding Formula No. 1**

Ingredients	Amount, Gm.	Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories
Dry skimmed milk powder	100	35.6	1	52	359
Water	750	...	...	...	...
Cream, 20%	150	4.3	30	6	311
Glucose	10	...	...	10	40
Strained liver	30	4.5	1	...	30
Stress formula vitamin concentrate†	1 capsule	...	...	...	...
Total		44.4	32	68	740

* Calculated on basis of 1,000 ml., with two-thirds calorie per milliliter.

† One capsule supplies thiamin hydrochloride, 10 mg.; riboflavin, 10 mg.; niacinamide, 100 mg.; ascorbic acid, 300 mg.; pyridoxine hydrochloride, 2 mg.; folic acid, 1.5 mg.; calcium pantothenate, 20 mg.; and vitamin B_{12}, 4 mcg.

After the nasogastric tube was passed, nothing was fed through the tube for the first eight hours, except several 50-cc. volumes of water to insure patency of the tube. For the second eight-hour period, saturated lime water was fed through the tube by giving 25 cc. per hour for the first four hours, then 50 cc. per hour for the second four hours. After this, feeding of the gastrostomy formula no. 1 (table 1) was started, first at the rate of 50 cc. per hour for four feedings and then 100 cc. per hour. Thereafter, in a 24-hour period, a total fluid intake of 2,400 cc. per day was given at the rate of 100 cc. per hour, which supplied 1,776 calories and adequate amounts of protein, fat, carbohydrate, and vitamins, as may be calculated from table 1.

Precautions were taken to have suction readily available at the bedside of these patients in the event of regurgitation or aspiration, and they were given careful nursing supervision. Routine blood testing and urinalyses were done, and nonprotein nitrogen, fasting blood sugar, total serum protein with albumin to globulin ratio, and electrolyte levels were determined at intervals throughout the period of study.

The patients reported here developed frequent loose stools after being on therapy with gastrostomy formula no. 1 for periods ranging from one to two weeks. The development of diarrhea greatly magnifies the nursing problem and enhances the chances of urinary tract infection and the development of decubitus ulcers. After diarrhea had developed, stool cultures were made and, in all cases, grew normal flora. Incidentally, none of these patients were treated with antibiotics during the period of the study. After diarrhea had become a troublesome problem for these patients, they were switched from the therapy with gastrostomy feeding formula no. 1 to that with the soy bean milk preparation.

The soy bean milk[1] used was prepared simply and on the ward merely by dilution of a can of soy bean milk with an equal volume of water. To this were added vitamins in the same amounts used for the gastrostomy formula (table 1). The mixture was stored at the bedside in ice until used. One can of soy bean milk so diluted provides 620 calories.

The feedings of soy bean milk were started at the rate of 50 cc. per hour; after a period of three days this amount was increased so that the patients were receiving, each 24 hours, between 2,400 and 2,790 cc., which provided between 1,600 and 1,860 calories with adequate amounts of protein, fat, and carbohydrate, as may be calculated from table 2.

The patients were continued on therapy with the soy bean milk preparation for a period of two weeks, blood testing done, as indicated above, at the start and end of the two-week period. These results are recorded in table 3.

Results

Of the nine patients switched to the soy bean milk therapy, five responded promptly within 36 hours, with a cessation of diarrhea and the passage of no more than two or three soft, but formed, yellow-brown stools. Two patients continued to have more frequent bowel movements, i. e., five or six per day, of poorly formed stools for the first three or four days on therapy with soy bean milk, after which their stools too were reduced in number to two or three per day.

TABLE 2.—*Composition of Soy Bean Milk (Mull-Soy)*

	Undiluted, %	Diluted with Equal Volume of Water,* %
Water	75.0	87.2
Soy protein	6.0	3.1
Soy fat	7.8	4.0
Carbohydrate	8.9	4.5
Crude fiber	0.3	0.2
Minerals		
Total	2.0	1.0
Calcium	0.26	0.13
Phosphorus	0.22	0.11
Iron	0.0004	0.0002
Calories per fluid ounce	40.0	20.0
Calories per cubic centimeter	1.33	0.66

* 1:1 dilution contains 16 mEq. of sodium per liter.

Two of the nine patients did not respond particularly well either to gastrostomy feeding formula no. I or to the soy bean milk. One of these patients occasionally regurgitated the feeding almost as soon as it was given, and great care had to be exercised to avoid aspiration pneumonitis. She also continued to have frequent, loose bowel movements. The other patient had loose, frequent bowel movements which were not altered by the use of soy bean milk but which were reduced in number by the use of paregoric, 5 cc. given four times a day. No patient given either tube feeding preparations showed distention or constipation or developed other gastrointestinal complications.

As can be seen from table 3, the blood chemistry levels remained stable during the period of feeding of soy bean milk. Further, there was no evidence of unfavorably altered clinical status of these patients during this study.

Comment

Although tube feeding is a life-conserving measure which must often be resorted to in patients who are comatose or who are unable to swallow, every possible effort should be used to attempt to get patients to swallow and take nutrients by the normal mechanism before tube feeding is employed. Tube feeding should be patterned to the need of the patient and not to the convenience of the doctor or nursing staff. The most serious and constant threat in a patient receiving tube feeding is the danger of regurgitation or vomiting, because their inadequate swallowing mechanism practically insures aspiration with its undesirable sequelae unless the patient is immediately given suction or positioned to prevent aspiration. For this reason, suction and close nursing supervision should be available for the tube-fed patient.

Table 3.—*Blood Analyses in Nine Patients with Gastrostomy Feedings*

Case No.	Sex	Age, Yr.	Nonprotein Nitrogen, Mg. %		Fasting Blood Sugar, Mg. %		Total Protein, Gm. %		Albumin, Gm. %		Globulin, Gm. %		Carbon Dioxide, mEq./Liter		Chlorides, mEq./Liter		Sodium mEq./Liter		Potassium, mEq./Liter	
			Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.
1................	F	65	42	38	82	86	6.20	6.44	3.21	3.10	2.99	3.34	26.7	28.0	94	93	141	137	5.1	4.8
2................	F	55	36	40	91	88	6.73	6.54	3.59	3.60	3.14	2.94	22.7	25.0	96	99	135	140	4.5	4.3
3................	M	72	42	39	62	70	8.20	7.82	2.48	2.58	5.72	5.24	30.1	29.0	104	97	144	140	4.1	3.8
4................	M	68	51	48	71	80	7.12	7.40	3.00	2.88	4.12	4.52	26.0	29.2	103	100	140	136	4.4	4.8
5................	M	71	31	35	68	75	5.82	6.24	2.56	2.40	3.26	3.84	21.0	26.0	92	94	130	134	4.8	4.1
6................	F	94	30	41	98	90	6.18	5.88	3.20	3.40	2.98	2.48	28.0	27.1	99	103	140	138	4.4	3.8
7................	M	78	48	46	58	79	5.64	5.86	2.34	2.38	3.30	3.48	24.0	22.1	94	98	130	134—	4.6	4.8
8................	F	82	59	61	62	68	7.20	7.00	3.10	3.00	4.10	4.00	20.0	19.8	103	106	135	141	4.0	4.4
9................	F	62	32	36	71	75	8.02	7.64	3.20	3.62	4.82	4.02	20.0	19.5	104	100	128	134	4.8	4.6

The experience reported here indicates that soy bean milk diluted 1:1 with water and supplemented with vitamins is a convenient, relatively inexpensive formula for tube feeding which is well tolerated by the patient and produces a minimum of gastrointestinal complications. It is a physiologically and nutritionally sound preparation which has had long and highly satisfactory usage, especially in pediatric medicine. The fact that its preparation is so simple and can be done on the ward by the nursing staff reduces the work of the usually overtaxed staff of the dietetics department. Further, the amount of the tube feeding preparation made at any one time can be small, thus eliminating spoilage, which may become a vexing problem with the usual specially prepared formulas.

It should be pointed out that, while soy bean milk fortified with vitamins and given as reported above is nutritionally adequate within the range of recommended dietary allowances, it is deficient in iron and, when used for a prolonged period of time, should be supplemented with this element. A most convenient form of iron which has been used for this purpose is iron choline citrate complex, prepared as pediatric drops,[a] which contains 16 mg. of elemental iron per cubic centimeter. Two cubic centimeters of this preparation is added for each can of soy bean milk diluted 1:1 with water.

The low sodium content, i. e., 16 mEq. per liter of the 1:1 dilution, provides an ideal dietary regimen when a low sodium intake is also needed in the management of the patient.

Summary

Nine patients in whom tube feeding had been used and in whom diarrhea became troublesome with the usual skim milk–based formula were given a soy bean milk preparation. This is simply prepared by dilution of a can of the ready-prepared soy bean milk with an equal amount of water and fortification with vitamins. The soy bean milk preparation for tube feeding was effective in returning the bowel movement pattern to normal limits in seven of the nine patients.

333 Cedar St. (11).

The soy bean milk preparation used in this study was supplied as Mull-Soy by the Borden Company, Prescription Products Division, New York. The iron choline citrate complex was supplied as Chel-Iron pediatric drops by Kinney & Company, Inc., Columbus, Ind.

References

1. Manual of Diets, Dietary Department, New Haven, Conn., Grace-New Haven Community Hospital, 1954.

2. Balfour, D. C., Jr.: Control of Stomach Pain, Am. J. Gastroenterol. **22**:181-191 (Sept.) 1954.

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4. Glaser, J., and Johnstone, D. E.: Soy Bean Milk as Substitute for Mammalian Milk in Early Infancy, Ann. Allergy **10**:433-439 (July-Aug.) 1952.

ing from three days to one week, and attempts were made routinely to establish whether they could swallow water without aspiration. When it had been established that the patients could not swallow sufficiently well to provide adequate nutrition, the intravenous therapy was discontinued and a nasogastric tube was passed in preparation for tube feeding. Two types of nasogastric tubes were used, i. e., a soft rubber Glenn tube and a small plastic Levin tube. The former tube is preferred because its soft, collapsible, pliable structure minimizes esophageal irritation.

TABLE 1.—*Analysis of Gastrostomy Tube Feeding Formula No. 1*[*]

Ingredients	Amount, Gm.	Protein, Gm.	Fat, Gm.	Carbohydrate, Gm.	Calories
Dry skimmed milk powder	100	35.6	1	52	359
Water	750	...	...	...	...
Cream, 20%	150	4.3	30	6	311
Glucose	10	...	...	10	40
Strained liver	30	4.5	1	...	30
Stress formula vitamin concentrate†	1 capsule	...	...	...	...
Total		44.4	32	68	740

[*] Calculated on basis of 1,000 ml., with two-thirds calorie per milliliter.

† One capsule supplies thiamin hydrochloride, 10 mg.; riboflavin, 10 mg.; niacinamide, 100 mg.; ascorbic acid, 300 mg.; pyridoxine hydrochloride, 2 mg.; folic acid, 1.5 mg.; calcium pantothenate, 20 mg.; and vitamin B_{12}, 4 mcg.

After the nasogastric tube was passed, nothing was fed through the tube for the first eight hours, except several 50-cc. volumes of water to insure patency of the tube. For the second eight-hour period, saturated lime water was fed through the tube by giving 25 cc. per hour for the first four hours, then 50 cc. per hour for the second four hours. After this, feeding of the gastrostomy formula no. 1 (table 1) was started, first at the rate of 50 cc. per hour for four feedings and then 100 cc. per hour. Thereafter, in a 24-hour period, a total fluid intake of 2,400 cc. per day was given at the rate of 100 cc. per hour, which supplied 1,776 calories and adequate amounts of protein, fat, carbohydrate, and vitamins, as may be calculated from table 1.

Precautions were taken to have suction readily available at the bedside of these patients in the event of regurgitation or aspiration, and they were given careful nursing supervision. Routine blood testing and urinalyses were done, and nonprotein nitrogen, fasting blood sugar, total serum protein with albumin to globulin ratio, and electrolyte levels were determined at intervals throughout the period of study.

The patients reported here developed frequent loose stools after being on therapy with gastrostomy formula no. 1 for periods ranging from one to two weeks. The development of diarrhea greatly magnifies the nursing problem and enhances the chances of urinary tract infection and the development of decubitus ulcers. After diarrhea had developed, stool cultures were made and, in all cases, grew normal flora. Incidentally, none of these patients were treated with antibiotics during the period of the study. After diarrhea had become a troublesome problem for these patients, they were switched from the therapy with gastrostomy feeding formula no. 1 to that with the soy bean milk preparation.

The soy bean milk[1] used was prepared simply and on the ward merely by dilution of a can of soy bean milk with an equal volume of water. To this were added vitamins in the same amounts used for the gastrostomy formula (table 1). The mixture was stored at the bedside in ice until used. One can of soy bean milk so diluted provides 620 calories.

The feedings of soy bean milk were started at the rate of 50 cc. per hour; after a period of three days this amount was increased so that the patients were receiving, each 24 hours, between 2,400 and 2,790 cc., which provided between 1,600 and 1,860 calories with adequate amounts of protein, fat, and carbohydrate, as may be calculated from table 2.

The patients were continued on therapy with the soy bean milk preparation for a period of two weeks, blood testing done, as indicated above, at the start and end of the two-week period. These results are recorded in table 3.

Results

Of the nine patients switched to the soy bean milk therapy, five responded promptly within 36 hours, with a cessation of diarrhea and the passage of no more than two or three soft, but formed, yellow-brown stools. Two patients continued to have more frequent bowel movements, i. e., five or six per day, of poorly formed stools for the first three or four days on therapy with soy bean milk, after which their stools too were reduced in number to two or three per day.

TABLE 2.—*Composition of Soy Bean Milk (Mull-Soy)*

	Undiluted, %	Diluted with Equal Volume of Water,[*] %
Water	75.0	87.2
Soy protein	6.0	3.1
Soy fat	7.8	4.0
Carbohydrate	8.9	4.5
Crude fiber	0.3	0.2
Minerals		
Total	2.0	1.0
Calcium	0.26	0.13
Phosphorus	0.22	0.11
Iron	0.0004	0.0002
Calories per fluid ounce	40.0	20.0
Calories per cubic centimeter	1.33	0.66

[*] 1:1 dilution contains 16 mEq. of sodium per liter.

Two of the nine patients did not respond particularly well either to gastrostomy feeding formula no. 1 or to the soy bean milk. One of these patients occasionally regurgitated the feeding almost as soon as it was given, and great care had to be exercised to avoid aspiration pneumonitis. She also continued to have frequent, loose bowel movements. The other patient had loose, frequent bowel movements which were not altered by the use of soy bean milk but which were reduced in number by the use of paregoric, 5 cc. given four times a day. No patient given either tube feeding preparations showed distention or constipation or developed other gastrointestinal complications.

As can be seen from table 3, the blood chemistry levels remained stable during the period of feeding of soy bean milk. Further, there was no evidence of unfavorably altered clinical status of these patients during this study.

Comment

Although tube feeding is a life-conserving measure which must often be resorted to in patients who are comatose or who are unable to swallow, every possible effort should be used to attempt to get patients to swallow and take nutrients by the normal mechanism before tube feeding is employed. Tube feeding should be patterned to the need of the patient and not to the convenience of the doctor or nursing staff. The most serious and constant threat in a patient receiving tube feeding is the danger of regurgitation or vomiting, because their inadequate swallowing mechanism practically insures aspiration with its undesirable sequelae unless the patient is immediately given suction or positioned to prevent aspiration. For this reason, suction and close nursing supervision should be available for the tube-fed patient.

TABLE 3.—*Blood Analyses in Nine Patients with Gastrostomy Feedings*

			Nonprotein Nitrogen, Mg. %		Fasting Blood Sugar, Mg. %		Total Protein, Gm. %		Albumin, Gm. %		Globulin, Gm. %		Carbon Dioxide, mEq./Liter		Chlorides, mEq./Liter		Sodium mEq./Liter		Potassium, mEq./Liter	
Case No.	Sex	Age, Yr.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.	Start	2 Wk.
1................	F	65	42	38	82	86	6.20	6.44	3.21	3.10	2.99	3.34	26.7	28.0	94	93	141	137	5.1	4.8
2................	F	55	36	40	91	88	6.73	6.54	3.59	3.60	3.14	2.94	22.7	25.0	96	99	135	140	4.5	4.3
3................	M	72	42	39	62	70	8.20	7.82	2.48	2.58	5.72	5.24	30.1	29.0	104	97	144	140	4.1	3.8
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6................	F	94	36	41	98	90	6.18	5.88	3.20	3.40	2.98	2.48	28.0	27.1	99	103	140	138	4.4	3.8
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The experience reported here indicates that soy bean milk diluted 1:1 with water and supplemented with vitamins is a convenient, relatively inexpensive formula for tube feeding which is well tolerated by the patient and produces a minimum of gastrointestinal complications. It is a physiologically and nutritionally sound preparation which has had long and highly satisfactory usage, especially in pediatric medicine. The fact that its preparation is so simple and can be done on the ward by the nursing staff reduces the work of the usually overtaxed staff of the dietetics department. Further, the amount of the tube feeding preparation made at any one time can be small, thus eliminating spoilage, which may become a vexing problem with the usual specially prepared formulas.

It should be pointed out that, while soy bean milk fortified with vitamins and given as reported above is nutritionally adequate within the range of recommended dietary allowances, it is deficient in iron and, when used for a prolonged period of time, should be supplemented with this element. A most convenient form of iron which has been used for this purpose is iron choline citrate complex, prepared as pediatric drops,[2] which contains 16 mg. of elemental iron per cubic centimeter. Two cubic centimeters of this preparation is added for each can of soy bean milk diluted 1:1 with water.

The low sodium content, i. e., 16 mEq. per liter of the 1:1 dilution, provides an ideal dietary regimen when a low sodium intake is also needed in the management of the patient.

Summary

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References

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INTRAVENOUS UROGRAPHY WITH RENOGRAFIN 60%

A REPORT OF MORE THAN 600 CASES

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The reliability and safety of intravenous urography were studied in 654 patients. The injection consisted of 25 cc. of Renografin (a 60% aqueous solution of the methylglucamine salt of 3,5-diacetylamido-2,4,6-triiodobenzoate) given over a period of three minutes; in only three cases were smaller doses used. There were no severe reactions, but vomiting occurred in 11 patients. One of these had a history of allergy, and another had not been properly prepared. The low incidence of reactions was striking because the ages of the patients ranged from 7 to 84 years and 16 had histories of allergy or severe reactions to previously administered contrast agents. Satisfactory roentgenograms of the kidneys were obtained in 636 (97%) of the cases, demonstrating the great diagnostic value of this procedure.

In the 30 years since Osborne and co-workers[1] first attempted to visualize the urinary tract in laboratory animals with intravenously given sodium iodide, intravenous urography has become a widely accepted clinical procedure in urologic diagnosis. According to one estimate, a total of 11,546,000 intravenous urographic procedures were performed in the United States alone from 1942 to 1956, the annual number increasing from 280,000 in 1942 to 1,368,000 in 1956.[2] This remarkable progress within a relatively short time—from laboratory experiment to universally employed diagnostic tool—has come about largely because of the successful development and introduction of new and improved contrast agents.

In 1928 Binz and Räth[3] and in 1930 Swick[4] reported the use of uroselectan after the discovery that selectan-neutral provided good contrast of the kidney, but its use was attended by toxic manifestations. In 1929, uroselectan B (Neo-iopax) was introduced, this being less toxic than uroselectan.[5] Several years later, iodopyracet (Per-abrodil [Diodrast]) was developed, and, for 20 years thereafter, iodopyracet and uroselectan B were commonly used in the majority of intravenous urographic procedures in the United States.[2] More recently, a number of new contrast mediums have been introduced in the United States, the most prominent being perhaps Hypaque and Urokon.

In 1955, a new, organic, tri-iodinated radiopaque compound, identified as Renografin, became available for clinical trial in intravenous urography. After preliminary trials of this material in both the 76 and 60% concentrations, results of which have been reported elsewhere,[6] Renografin 60% has been used exclusively at this clinic for intravenous urography in ambulant patients. Individual case reports have been recorded at the time of examination of each patient, with particular attention to signs of sensitivity or other reaction or vessel pain and to the quality of the urograms obtained with this medium. From April, 1957, to the time of this report, over 600 patients were examined with Renografin 60%. Urograms of diagnostic quality have been consistently obtained with practically no side-effects. The purpose of this communication is to describe briefly our experience with Renografin 60% at this large private clinic during the past year and a half.

Methods and Materials

Patients.—A total of 654 patients is included in this report, 394 male and 260 female. They ranged in age from 7 to 84 years and in weight from 50 to 255 lb. (22.7 to 115.6 kg.). Sixteen patients had a history of hay fever, asthma, or severe reaction to previously administered contrast agents. Each of the 654 patients had presented signs or symptoms of disorders related to the urinary tract or renal pelvis and had been referred to the clinic for diagnosis. The distribution of the patients with reference to age, sex, and weight appears in table 1.

Contrast Medium.—Renografin 60% contains 60% of the methylglucamine salt of 3,5-diacetylamido-2,4,6-triiodobenzoate (diatrizoate) in aqueous solution adjusted to neutrality with sodium hydroxide. The solution contains approximately 29.26% iodine.

Method of Study.—Prior to examination, standard instructions for preparation were given to each patient. Each was advised to take 12 fl. oz. (360 cc.) of magnesium citrate solution 36 hours before coming for examination to eat lightly the day before, and, after midnight, to take nothing by mouth except coffee and toast for breakfast. (Eight patients were examined without such preparation.)

In earlier studies with Renografin, a preliminary test dose of 1 cc. was routinely administered to each patient before examination. In the absence of any reaction whatsoever, use of the test dose was finally abandoned. In fact, none was given to any patient in this series.

At examination, 25 cc. of Renografin 60% was given intravenously over a period of three minutes to every patient, with three exceptions. Only 15 cc.

was given to two boys aged 10 and 13 years, respectively, and 10 cc. was given to an adult patient who had had a severe reaction to a previously administered dye and was apprehensive about the possibility of a similar reaction to Renografin—which did not occur. Films were exposed at 5, 10, and 15 minutes after injection, with the patient erect at the final film. The resulting urograms were evaluated and classified as excellent, good, and fair (there were no poor films), mainly on the basis of the presence or absence of a clear-cut pyelogram in good density, regardless of the age, weight, kidney function, or lack of preparation of the patient.

Table 1.—*Data from 654 Patients Subjected to Intravenous Urography with Renografin 60%*

	No. of Patients		
Age, Yr.	Male	Female	Total
0-10	5	1	6
11-20	18	8	26
21-30	19	46	65
31-40	38	65	103
41-50	71	42	113
51-60	92	42	134
61-70	84	34	118
>70	67	21	88
Not recorded	0	1	1
Total	394	260	654
Weight, Lb.			
<100	12	12	24
100-110	3	42	45
111-120	7	37	44
121-130	20	30	50
131-140	32	57	89
141-150	57	37	94
151-160	51	13	64
161-170	56	12	68
>170	152	19	171
Not recorded	4	1	5
Total	394	260	654

Results

A summary appears in table 2 of the quality of films obtained with Renografin 60% and the associated reactions encountered. It is evident from this table that good to excellent delineation of the renal collecting system was achieved in 636 of the 654 cases, while only a fair outline was demonstrated in the remaining 18. As anticipated, the greatest proportion of satisfactory films was seen in younger persons of lighter weight. The excretory capacity as a rule is better in younger subjects. Older patients are more difficult to prepare for urographic examination. Moreover, in older persons intestinal gas often obscures and sometimes blocks out kidney delineation even though the dye may be present in the kidney in sufficient concentration to give a good contrast. The quality of films obtained in the individual patients with reference to their respective ages and weights appears in table 3.

Table 2.—*Summary of Results in Intravenous Urographic Examination with Renografin 60%*

	Total No. of Patients			No. of patients Showing Reactions		
Quality of Films	Male	Female	Total	Male	Female	Total
Excellent	62	44	106	3	7	10
Good	318	212	530	14	14	28
Fair	14	4	18	2	0	2
Total	394	260	654	19	21	40

Table 3.—*Quality of Films Obtained with Renografin 60% with Reference to Age and Weight*

	Quality of Films (No. of Cases)			
Age, Yr.	Excellent	Good	Fair	Total
0-10	6	18	0	6
11-20	7	19	0	26
21-30	23	40	2	65
31-40	28	75	0	103
41-50	21	87	5	113
51-60	15	114	5	134
61-70	8	107	3	118
>70	2	83	3	88
Not recorded	0	1	0	1
Total	106	530	18	654
Weight, Lb.				
<100	6	18	0	24
100-110	10	34	1	45
111-120	11	31	2	44
121-130	6	42	2	50
131-140	10	74	5	89
141-150	11	82	1	94
151-160	9	53	2	64
161-170	11	56	1	68
>170	29	139	3	171
Not recorded	3	1	1	5
Total	106	530	18	654

There were no severe reactions in any patient in the entire series. A total of 40 patients reported 58 different reactions to the dye, but these reactions were relatively mild and transient in every case. Of the 40 patients with reactions 4 had a history of allergy; 2 had not received the standard preparation prescribed before examination. The incidence of reactions encountered in this study is given in table 4.

Table 4.—*Incidence of Reactions in Forty Patients Subjected to Intravenous Urography with Renografin 60%*

Reaction	Patients,* No.	History of Allergy, No.	Unprepared for Examination,† No.
Nausea	32	2	2
Vomiting	11	1	1
Choking sensations	2	0	
Flushing of skin	8	0	
Tingling of extremities	2	0	
Itching sensations	1	0	
Urticaria	1	0	
Sneezing	1	1	
Total	58	4	8

*Same patient reported one, two, or even three different reactions in number of instances.

†Same patient reported nausea and vomiting in one instance.

Comment

The relatively few and mild reactions encountered in this series is the most striking feature of this study. It is hard to believe that any drug introduced intravenously could be so well borne by so many patients as has Renografin 60% in this large series. The rate of occurrence of reactions is 6%

(40 of 654 patients), which is in accord with the reaction rate reported by others using this medium.[7] Since films of good or excellent quality were obtained in a high percentage (97%) of the cases examined with Renografin 60%, this contrast agent is obviously satisfactory for use in intravenous urography.

Summary and Conclusions

Intravenous urographic examinations have been conducted in a total of 654 patients with use of Renografin 60% as the contrast agent. Satisfactory films were obtained in 636 (97%) without serious reactions to the medium. Mild reactions, such as nausea, vomiting, a sensation of itching, flushing of the skin, urticaria, sneezing, and a choking sensation, were reported by a total of 40 patients.

On the basis of the high percentage of good or excellent films obtained with Renografin 60% and the remarkably few and mild reactions encountered, it is concluded that Renografin 60% is a superior contrast agent for intravenous urography in the ambulant patient.

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BRONCHIAL ASTHMA DUE TO FOOD ALLERGY ALONE IN NINETY-FIVE PATIENTS

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and
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The assumption that bronchial asthma is due to inhaled allergens, such as the pollens, has sometimes resulted in overlooking allergens in food. Food allergy has too often been ignored or inadequately controlled when it was the sole cause of bronchial asthma or contributed to the effects of inhaled allergens. Recognition of the importance of food allergy in a given patient is usually impossible unless one begins with a cereal-free elimination diet which assumes allergy to cereal grains as well as to milk, eggs, and other less common allergenic foods. This was clearly demonstrated in 50 children and 45 adults, whose bronchial asthma was relieved without use of antigens, vaccines, corticosteroids, or ACTH. Strict adherence to the diet was necessary at first, especially in the winter, but in many cases it was found that tolerance to some foods developed in one to four years and that a more liberal diet could be allowed in the summer.

Bronchial asthma due to food allergy[1] alone or associated with inhalant allergy is too frequently overlooked. This is due to failure to recognize the typical history of bronchial asthma due to food allergy,[2] especially in children, and its equivalent in adults, including older persons, as summarized below. It also results from the frequency of negative skin reactions to foods causing the asthma[3] and the usual failure of positive skin findings to reveal the responsible foods. Thus, most diets excluding foods giving positive skin reactions fail to control bronchial asthma due to food allergy.[3A] Our realization of the frequency of food allergy therefore has depended on trial diets, of which our cereal-free elimination diet[4] has been most important. Our success has depended on the elimination of all cereal grains, along with milk, egg, chocolate, fish and other less common allergenic foods. Recurrent colds and bronchitis with or without slight wheezing during the fall, winter, and spring months also require similar study of food allergy, as revealed by good results with its use.

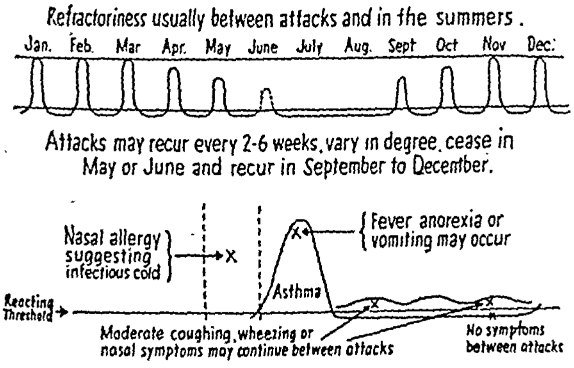
Read in the Session on Allergy before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 27, 1958.

Our emphasis on food allergy does not detract from the equally important inhalant allergy [5] alone or in association with food sensitization. The role of pollen allergy in asthma limited to the pollen seasons and the importance of animal emanations, house dusts, miscellaneous inhalants, and fungi must be remembered. Positive skin reactions to inhalants, however, do not predetermine clinical allergy. Assurance of such allergy requires long-lasting relief of asthma with desensitization therapy and/or environmental control. Unnecessary and, at times, prolonged ineffectual desensitization to inhalants too often has preceded the relief of bronchial asthma arising from our cereal-free elimination diet.

This increased recognition of food allergy as the cause of bronchial asthma [1a] has minimized possible *bacterial infection or allergy* [5A] as the cause, as reported by Cooke,[6] Chobot [7] and other allergists. The occurrence of viral or infectious colds and bronchitis without resultant asthma [1] when *it is* controlled with elimination of causative foods supports our conclusion that infection is a rare cause of the recurrent bronchial asthma.

Typical History

Recurrent bronchial asthma [8] every two to six weeks, being moderate or severe for one to three days, diminishing in the subsequent one to five days, and decreasing or absent in the summer always suggests food allergy (see figure). It usually starts in the first three years, though a similar or equivalent history occurs in adult life and old age. Initial nasal symptoms suggesting an infectious cold, often with slight fever, generally are wrongly attributed to infection rather than food allergy as the cause. Moderate or severe bronchial asthma then occurs for one to three days with a gradual decrease in one to five days. Fever, due to food allergy, up to 104 F (40 C), is frequent. Anorexia and vomiting may occur. Antibiotics, sulfonamides, and gamma globulin therefore are infrequently justified. Exhaustion of assumed reacting bodies to the allergenic foods terminates the attack. With their regular reaccumulation to the reacting level, attacks recur. Absence of reacting bodies between attacks allows the ingestion of allergenic foods without asthma. If they are not entirely exhausted, slight, interim symptoms may occur. Tolerance for the allergenic foods may develop if the food allergy is controlled for one to four years.


Refractoriness usually between attacks and in the summers.
Jan.
Feb.
Mar
Apr.
May
June
July
Aug.
Sept
Oct
Nov
Dec.
Attacks may recur every 2-6 weeks, vary in degree, cease in May or June and recur in September to December.
Nasal allergy suggesting infectious cold
X
Fever anorexia or vomiting may occur
Asthma
Reacting Threshold
Moderate coughing, wheezing or nasal symptoms may continue between attacks
No symptoms between attacks

Recurrent attacks of bronchial asthma due to food allergy, especially in children.

TABLE 1.—*Bronchial Asthma Due to Food Allergy Alone in Infants and Children (Fifty Cases)**

Males, %	66	
Females, %	34	
Age, yr. (av., 5.1)	3/4-13	
Age at onset, yr. (av., 1.6)	1/6-6	
Time with asthma, yr. (av., 3.4)	1/4-9	
Duration of attacks, days	2-10	
Typical history, %	74	92
Less typical history, %	18	
"Cold" at onset of attack, %	78	
Fever with attacks (under 101 F), %	38	60
Fever with attacks (101-105 F), %	22	
Vomiting with attacks, %	36	
Attacks absent in summer, %	44	82
Attacks decreased in summer, %	41	
Symptoms between attacks		
Nasal, %	58	
Bronchial, %	36	
Former nasal allergy, %	18	
Former eczema, %	38	
Former GI symptoms, %	44	
History of possible food allergy, %	50	
Family history of possible allergy, %	80	
Eosinophilia (blood), % (av., 5.4)	0-19	
Skin reactions		
Foods, %	52	
Pollens,† %	30	
Animal emanations,† %	20	
Miscellaneous,† %	4	
House dust,† %	26	
Av. time of supervision, yr.	1.8	

* No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.

†No therapy based on skin reactions.

That infection is not the cause is evidenced by the occurrence of true infectious colds or even pneumonitis with no asthma if the allergenic foods are eliminated. Recurrent colds, with or without coughing and with little or no wheezing, also are often due to food allergy alone rather than infection.

Children.—To emphasize food allergy as a sole cause of bronchial asthma, the statistics in table 1 on 50 infants and children are presented to show bronchial asthma controlled with the elimination of allergenic foods without any injections of inhalant allergens or vaccines and with no corticosteroids, ACTH, antibiotics, or chemotherapy. Many more cases due to food allergy alone are omitted because of brief or longer injections of antigens or vaccines which we now realize were unnecessarily given, largely because of positive skin reactions. A few cases due to food allergy are not included either, because injections of gamma globulin were given and this is of unproved value in asthma.[9] Though antibiotics and chemotherapy are not indicated during attacks of asthma due to food allergy alone, it is justifiable to give such medicaments and respiratory vaccines to help infrequent, secondary infections in such asthma-free persons in all age groups.

The classic or nearly typical history of bronchial asthma due to food allergy is seen to have occurred in 92%. Initial "colds" suggesting infection but due to food allergy occurred in 78%. Antibiotics and sulfonamides had been given ineffectively to some patients for months or years because of assumed infection. Previous fever in 60% and vomiting in 36% did not occur with our control of food allergy. The asthma was decreased or absent in summer in 82%.[10] Slight nasal symptoms in 58% or bronchial symptoms in 36% between previous attacks were relieved with the elimination diet. The former eczema, blood eosinophilia, and recurrent colds were probably results of food allergy. Negative [illegible] in 48%. The [illegible] gave little or no help in our [illegible]. The positive reactions to [illegible] or due to potential [illegible] since the control of food allergy [illegible] relief. Diet history of food [illegible] correlated with the clinical [illegible] in a few patients, especially in cases of [illegible] sensitization. Family histories of prob- [illegible] at times only in aunts, uncles, or grand- [illegible] of asthma or "sinus trouble" oc- [illegible]

[illegible] from parents reflected the importance of the control of food allergy in bronchial asthma in children and indicated that satisfactory results were obtained with the elimination diet alone.

Adults 15 to 55 Years of Age.—The classic history of bronchial asthma due to food allergy occurs in some adults.[11] Usually the asthma is perennial, decreasing or infrequently absent in the summers. Though interim relief between attacks is less than that in children, careful interrogation usually reveals cyclic exaggeration of the chronic asthma, due, in our opinion, to intermittent activation of the causative food allergy. Fever due to food allergy[12] is infrequent in these adults as compared with children. When present, especially if it is prolonged, infrequent secondary infections also have to be considered. The importance of adequate study of allergy in perennial bronchial asthma usually exaggerated from autumn to spring was dramatized in a young woman with such asthma for several years. Finally it persisted without relief from November to March, when a right lower lobectomy was done for assumed questionable bronchiectasis. Because of postoperative infection, decortication of the right lung was necessary after six weeks. The severe asthma continued for four months until our study indicated probable food allergy. With the cereal-free elimination diet, relief occurred in one month and has continued to the time of writing. Such control of food allergy relieved the patient in another case in which lobectomy also had been advised on the basis of questionable x-ray and bronchoscopic findings. As in children, recurrent head and especially bronchial "colds" particularly from autumn to late spring are often relieved with the routine and accurate use of the cereal-free elimination diet, disproving infection as the cause.

TABLE 2.—*Bronchial Asthma Due to Food Allergy Alone in Thirty Adults 15 to 55 Years of Age**

Male, %	43	History suggestive of	
Female, %	57	Food allergy, %	50
Age, yr. (av., 34.8)	17-53	Inhalant allergy, %	0
Age at onset, yr. (av., 20.8)	1/2-47	Family history, %	46
Duration, yr. (av., 14)	1/2-39	Asthma, %	40
Perennial symptoms, %	100	Nasal allergy, %	20
Recurrent attacks, %	50	Cutaneous allergy, %	3
Worse in winter, %	47	Headaches and GI symptoms, %	3
Absent in summer, %	0	Skin reactions (scratch method)	
Better in summer, %	40	Foods, %	20
Better [illegible]	10	Pollens,† %	50
Other		Animal emanations and miscellaneous,† %	43
Nasa[illegible]	80	House dust,† %	36
Nasal polyps, %	10	Eosinophilia (blood), % [illegible]	9.8
Eczema, %	10		
Hives, %	10		
GI symptoms, %	10		
Headaches, %	5		

* No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.

†No therapy based on skin reactions.

If inhalant allergy, especially pollen, is associated with food allergy, the usual decrease or absence of symptoms in the summer[10] when food is the sole cause may not be observed. Recurrent asthma due to food with more persistent asthma from spring to late fall, moreover, occurs in the same patient.

Statistics on 30 cases of bronchial asthma due to food allergy in adults are given in table 2.

Because of the perennial, usually recurrent, exaggerated asthma, food allergy was studied with our cereal-free elimination diet before any injectants were given. With strict cooperation, relief was evident in one to four weeks. Manipulation of the diet thereafter gradually revealed the foods responsible for the asthma. This stresses the importance of recognizing food allergy and the futility of desensitization and vaccine therapy in such cases. It is rare today, however, that patients with perennial bronchial asthma are not given injectant therapy and that any adequate control of food allergy occurs. In several of these patients, such injections had been given for one to three or more years before our study of food allergy improved or controlled the asthma in one to four weeks.

As in children, skin reactions to foods infrequently correlated with clinical allergies. Moreover, therapy based on the recorded positive reactions to inhalants was not required.

In these adults the average age when first seen was 34.8 years. The age of onset of asthma was 20.8 years. Nasal allergy occurred in 80%. Asthma was worse in the winter in 47%. In the family history, the predominating clinical allergy was bronchial asthma in 40%. Blood eosinophilia occurred in 9.8%.

Adults Over 55 Years of Age.—For many years we have reported bronchial asthma due to food allergy in older patients.[13] Inhalant allergy with or without food allergy has been of similar importance. This refutes opinions of other allergists that inhalant and especially food allergies are rare or even absent, especially after the age of 50 years. In 1947 we reported 173 patients relieved of bronchial asthma who were over 55 years of age.[14] In 82%, food, inhalant, and rare bacterial allergy were causative; 40% were due, in our opinion, to food allergy alone. Thus food and inhalant allergies by our analyses were of equal importance.

In table 3 statistics are presented on 15 patients over 55 years of age with bronchial asthma controlled by the elimination of specific foods alone. This group would have been greater if we, like the majority of physicians, had not given unwarranted injections of inhalants or vaccines because of positive skin reactions or assumed infection. Moreover, cases of asthma exaggerated or occurring only in the fall, winter, and spring which were controlled with the use of our cereal-free elimination diet but in which pollen therapy was given because of active or potential pollen sensitization from late spring to fall are not included. In the last few years we have refrained from such injectant therapy when food allergy seemed to be the sole cause of the asthma and after it was adequately controlled with the elimination diet alone.

Bronchial asthma in 15 patients over the age of 55 years was controlled only with the elimination of allergenic foods. In spite of slight to moderate reactions to inhalants, no injections of antigens or vaccines were given. Asthma had existed for four months to 54 years with an average of 10 years. The age of onset was from 2 to 57 years with an average age of 50 years. Asthma was perennial except in one case. As in the classic history of asthma due to food allergy in children, the asthma was better in 46% and absent in one case in the summer months. There was no complete interim freedom between attacks, though recurrent exaggeration of asthma was evident in the histories of 40%. Improvement occurred in the summer in 40% and in dry, inland areas in 13%.[10] Nasal allergy had occurred in 66%. Drug allergy, especially to aspirin, occurred in 20%. Corticoids and/or ACTH had been given with no benefit to 20% of these patients before they were relieved with our elimination diets. They were not included in our results. Infective and intrinsic causes had been erroneously assumed *in several of these patients.*

Thus food and/or inhalant allergies must be studied in all patients with bronchial asthma in old age. Recognition of cardiovascular and renal disease, emphysema, and other causes of wheezing and dyspnea is necessary, of course, especially in this age group. Complete relief of such cases of bronchial asthma or asthmatic bronchitis, exaggerated or only occurring from fall to spring, minimizes possible infective or intrinsic causes. Only death terminates the development or continuance of such allergies in old age.

Study and Control of Food Allergy

Food allergy requires study when the classic history of bronchial asthma due to food allergy in childhood or similar or less typical perennial histories in adults and old age occur. It is also necessary when food and inhalant allergies are indicated causes.

To study and control food allergy, a diet which excludes foods that give large scratch reactions and/or a history of definite food dislikes or disagreements may be effective. The intradermal method of testing is not used in our study because of the many indefinite or false reactions which arise. Relief infrequently results because of the known fallibility of skin testing,[3A] especially in food allergy, and the frequent failure of diet histories to indicate any or all allergenic foods.

The cereal-free elimination diet[4] is then given, with indicated modifications. Indeed, it is usually used without the initial elimination of foods giving positive skin reactions or a positive diet history.

For good results, strict adherence to the diet is imperative, with maintenance of proper weight and nutrition. Realization that foods remain in the body for several days or longer is important. This, together with the time necessary for the disappearance of changes in the lungs, especially in chronic bronchial asthma, explains the time required for control of symptoms. Because of these facts a moderate attack may occur in one to three weeks after the start of the diet free of allergenic foods. The next expected attack, however, should be absent. If food allergy causes persistent or interim symptoms, some relief may not be evident for 5 to 10 days.

Inhalation of odors of allergenic foods must be minimized or avoided. The absence or decrease of symptoms due to food allergy during the summer and the increase in the fall, winter, and early spring months must be remembered.[10] This usually allows a liberal summer diet and requires a strict winter elimination diet to control the food allergy. Injections of inhalants or vaccines should not be given when food allergy is the probable or proved cause. If the cereal-free elimination diet fails to relieve asthma in three to four weeks, however, then such injections are justified if the history with or without positive skin reactions indicates inhalant allergy. Needless injections of inhalants or vaccines are costly and tend to decrease the importance of food allergy and the required elimination diet in the minds of patient and physician alike.

TABLE 3.—*Bronchial Asthma Due to Food Allergy Alone in Fifteen Patients over 55 Years of Age**

Male, %	66
Female, %	34
Age, yr. (av., 60)	55-70
Age at onset, yr. (av., 50)	2-57
Duration, yr. (av. 10)	1/3-54
Recurrent attacks, %	40
Perennial, %	93.4
Worse from fall to summer, %	46
Absent in summer, %	6.6
Better in summer, %	40
Better inland, %	13
Other manifestations of allergy	
Nasal allergy, %	66
Polyps, %	13
Hives, %	13
History suggestive of	
Food allergy (especially milk), %	66
Drug allergy, %	20
Inhalant allergy, %	0
Family history	
Bronchial asthma, %	26
Nasal allergy, %	13
GI symptoms, %	13
Skin reactions	
Food, %	33
Pollen,† %	40
Animal emanations and miscellaneous,† %	33-1/3
House dust,† %	20
Eosinophilia (blood), % (2-32)	8.3
Duration of cooperation, yr. (2.2)	1/2-10

* No antigens, vaccines, corticosteroids, ACTH, or routine antiasthmatic drugs given. Antibiotics and chemotherapy given only for infrequent secondary infections and not routinely during attacks.

†No therapy based on skin reactions.

Until relief of symptoms occurs from the elimination of allergenic foods or when symptoms recur from breaks in the diet or trial ingestion of causative foods, severe, at times intractable, asthma from food allergy requires epinephrine given hypodermically, aminophylline by vein or rectum, corticosteroids, ACTH, and adequate replacement of fluid and electrolytes. Less severe attacks or persistent symptoms require epinephrine given subcutaneously or by inhalation, aminophylline, ephedrine, and, if necessary, corticosteroids. Other inhalant therapy and, at times, antihistamines, isoproterenol (Isuprel), and iodides may be helpful.

The cereal-free elimination diet should be ordered immediately if the history gives any suggestion of food allergy. If nausea is present, parenterally given fluids and the preparation of the diet in a liquid or soft form are indicated until the appetite returns. The immediate use of the diet will hasten the control of food allergy and the discontinuance of the above medication.

As long as symptoms continue to require medication, physicians are challenged with the study and control of possible allergy to other foods, to inhalants, or to rarer infectants and drugs. Errors in the diet must always be suspected. When inhalant, drug, or rare infectant allergies accompany food allergy or are sole causes, their study and control obviously are necessary. The control of bronchial asthma with antiallergic therapy alone without medication is the physician's responsibility.

Summary

Food allergy as the sole cause of bronchial asthma or associated with inhalant or rare infectant or drug allergy is too often ignored and inadequately controlled by the medical profession. The classic history consists of regularly recurring attacks of bronchial asthma, usually preceded by nasal allergy suggesting an infectious cold rather than the causative food allergy. The attacks recurring from fall to late spring are often associated with vomiting and fever due to food allergy. The asthma decreases or is absent in the summer. It usually starts before the third year, though a similar history may begin in adult life or old age. Interim relief between the attacks is usual in childhood, decreasing in adolescence and in adult life.

The use of antibiotics and/or sulfonamides during attacks or daily for months or even years and the recent injections of gamma globulin for wrongly assumed infective asthma are unnecessary, costly, and of potential danger. Continued or intermittent corticosteroid therapy is unnecessary when food allergies are controlled.

In 50 children, 30 adults, and 15 older persons, relief was achieved without use of antigens, vaccines, corticosteroids, or ACTH. A larger number of such cases could have been reported had we not been tempted to inject inhalants and vaccines needlessly in cases we now realize were due to food allergy alone. Food allergy associated with inhalant allergy as a minor or major cause is also too often unrecognized. Bronchial asthma due to inhalants alone is frequent.

Recognition of the classic history of bronchial asthma due to food allergy and its control in children, adults, and in older persons has depended on our initial use of the cereal-free elimination diet which assumes allergy to cereal grains, as well as to milk, egg, and other less common allergenic foods. Strict adherence to this diet and maintenance of protein requirements and weight are necessary. The decrease or entire suppression of food allergy in the summer with exaggeration in the fall, winter, and early spring frequently allows a liberal diet in the summer compared with a strict elimination diet in the winter. Tolerance for foods may arise in one to four years, or such a diet in the winter may be required for many years.

The control of bronchial asthma with corticosteroids, ACTH, and other new and old drugs without the adequate and persistent study of allergenic causes and especially of the usually neglected food allergy is unscientific. It unfortunately ignores the responsibility of the profession to recognize and control atopic allergy which is causative in practically every patient.

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HEART DISEASE SCREENING IN ELEMENTARY SCHOOL CHILDREN

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A screening program for the purpose of estimating the prevalence rates for congenital and rheumatic heart disease was carried out among 6,311 children between the ages of 6 and 11 years. Among 165 children thus identified as requiring further study, a secondary program of examinations was carried out. The abnormalities discovered included 33 cases of congenital and 7 of rheumatic heart disease. The study revealed 29 cases of previously unrecognized cardiac abnormality but also relieved at least 15 children of a false diagnosis of heart disease. It was valuable not only in assuring some children of needed treatment but also in determining the diagnostic value of various physical findings.

Pediatric heart disease, in contrast to adult heart disease, is almost invariably associated with chamber enlargement or signs of abnormal cardiac function which enable the abnormal condition to be discovered if sought. Heart disease screening programs are a productive enterprise when conducted among children in a thorough fashion and directed toward detection of the congenital and rheumatic heart defects which are prevalent to varying degrees in various age groups. For instance, congenital heart disease is more prevalent among younger children than among adolescents for the reason that most children with severe defects die before adolescence is reached, although this is counteracted somewhat by the fact that certain of the acyanotic left-to-right shunts (in particular, atrial septal defect) are often not possible to diagnose until the age of 8 to 10 years or even until adolescence. Rheumatic heart disease usually does not appear until 7 to 10 years and is increasingly more prevalent thereafter with advancing age. Thus, there is a difference in the prevalence rates of rheumatic heart disease between populations of younger and older children. The over-all prevalence rate for organic heart disease in children of all ages should be roughly the same, with perhaps a slightly increased rate in adolescents as compared with preschool-aged and elementary school children.

This report is the first of three which will deal with different facets of the entire problem of mass screening for heart disease in children. This paper deals primarily with the results of a screening program in one community and its environs. Prevalence rates of heart disease and innocent murmurs are given, with a discussion of types of disease found, problems encountered, and suggested improvements. The second paper appears on page 1169 of this issue and deals with a comparison of three methods of primary mass screening for heart disease used in two communities. Specificity, sensitivity, efficiency, definitions, and performances are discussed. The third paper [1] compares methods and results of screening programs in two western Colorado communities (different populations than in the second paper), and these results, in turn, are compared with those of previous screening programs by others.

Method

The screening program to be described was conducted in Mesa County in western Colorado. The county has a population of about 35,000 to 40,000 persons, of whom about half live in Grand Junction, which is at an elevation of 4,575 ft. above sea level. There is an active, well-staffed county health department and a conscientious, alert medical society. The screening program was coordinated by a physician from the Colorado State Department of Public Health and financed by the Colorado Heart Association.

As many as possible of the accessible elementary school children in the county received a physical examination limited to inspection of the jugular venous pulsations in the neck, palpation of the radial and femoral pulses, inspection and palpation of the chest, auscultation of the heart with the subject in several positions, and blood pressure recordings from the arms and legs if indicated. This comprised the primary screening procedure and was performed by a total of 13 physicians who were experienced in pediatric cardiac auscultation and who worked in teams to facilitate frequent consultations. In addition, lead V_3R electrocardiographic tracings [2] and 70-mm. chest x-rays were obtained from about two-thirds of the children. Three portable electrocardiographs and the state mobile x-ray unit were used for these procedures.

With the Heart Disease Control Program, U. S. Public Health Service, assigned to the Colorado Sta [illegible] Health (Dr. Morton); Director, Mesa County [illegible] Public Health (Dr. Beaver); and Chief, Hear [illegible] U. S. Public Health Service (Dr. Arnold). Dr. Morton is now a resident in medicine at San Mateo County Community Hospital, San Mateo, Calif.

The primary screening phase of the program took place in the Mesa County schools on school days only; it lasted three weeks and covered 6,311 children, most of whom were in the first six grades. All nursing services and organization of volunteers from the Parent-Teacher Association were provided by the Mesa County Health Department. Twenty-seven schools were covered at 12 separate examining stations, in which children from outlying or smaller schools were brought by bus to the larger and more centrally located schools.

Table 1.—*Age and Sex Distribution of All Children Screened for Heart Disease in Mesa County, Colorado*

	Age, Yr.										
	5	6	7	8	9	10	11	12	13	14+	Total
Male, no. ...	33	442	498	517	526	543	489	145	27	5	3,225
Female, no. .	35	428	491	539	478	510	481	101	19	4	3,086
Total	68	870	989	1,056	1,004	1,053	970	246	46	9	6,311

A secondary screening procedure was also carried out in which all children who were thought to have heart disease or to need further evaluation to rule out the presence of heart disease were reexamined by an experienced pediatric cardiologist who was able to utilize complete history, physical examination, electrocardiogram, full-size chest x-ray, and fluoroscopy. Suspicion aroused by results of any of the three screening methods was enough to insure reexamination. This phase of the program required five full days to reexamine 165 children and was followed by letters describing the findings which were sent to the respective personal physicians (M.D.'s and otherwise) in the community.

Table 2.—*Comparison of Age and Sex With Diagnostic Categories*

			Diagnoses, No.					
			Heart Disease					
Age, Yr.	Sex	Normal	Congenital	Rheumatic	Other	ECG Abnormality	Past Rheumatic Fever	Total
5.....	M	33	0					33
	F	34	1					35
6.....	M	438	2	1			1	442
	F	427	0	1			0	428
7.....	M	492	2				4	498
	F	484	2				5	491
8.....	M	507	3	0		1	6	517
	F	530	4	1		1	3	539
9.....	M	524	1			1	0	526
	F	465	2			0	11	478
10.....	M	526	10		1		6	543
	F	508	1		0		1	510
11.....	M	487	1	0			1	489
	F	468	3	2			8	481
12.....	M	144					1	145
	F	100					1	101
13.....	M	26		1			0	27
	F	17		1			1	19
14+.....	M	4	0				1	5
	F	3	1				0	4
Totals.....	M	3,181	19	2	1	2	20	3,225
	F	3,036	14	5	0	1	30	3,086
Both sexes.....		6,217	33	7	1	3	50	6,311

Results

Of a total population of 6,604 children who were in the first six grades at this time (including two kindergarten classes and a class for retarded children), 6,311 (95.6%) were subjected to a physical examination. There is no information available to characterize the 294 children not examined.

Table 1 reveals a fairly even age and sex distribution for children aged 6 to 11 years, indicating a representative population for these ages. A total of 33 cases of congenital heart disease and 7 of rheumatic heart disease, in addition to several other types of abnormalities, was discovered. Table 2 presents this information in tabular form.

The 33 cases of congenital heart disease included 7 of atrial septal defect, 6 of pulmonary stenosis, 4 of ventricular septal defect, 4 of aortic stenosis, 3 of patent ductus arteriosus, 2 of coarctation of the aorta, and 1 of atrial septal defect combined with pulmonary stenosis. In addition, there was one child with unmistakable arachnodactyly (Marfan's syndrome) who had no detectable heart lesion as yet, one with dextrocardia (with situs inversus), and four with definite congenital heart disease, type undetermined pending cardiac catheterization. In three children a right-sided aortic arch was associated with the primary defect; one had aortic stenosis, one had atrial septal defect, and the other had dextrocardia. The seven children with rheumatic heart disease included five in whom only the mitral valve was involved, one with only the aortic valve involved, and one with both mitral and aortic valves involved.

The child with "other heart disease" was a boy with a long history of severe asthma who was diagnosed as having cor pulmonale on the basis of electrocardiographic evidence of right ventricular hypertrophy. The cor pulmonale could well be reversible and may disappear, since the asthma had no longer been acute during the past year and a half. The three children with electrocardiographic abnormality included one with isolated complete right bundle-branch block (without evidence of right ventricular hypertrophy) and two with anomalous muscle bundle between atrium and ventricle (Wolff-Parkinson-White Syndrome).

In addition, there were 50 instances of positive past history of acute rheumatic fever. These 50 cases must not be regarded as any basis for prevalence estimates, since this information was gathered as best it could be from several sources and there is no way of checking the reliability of a history of rheumatic fever.

A certain percentage of these cases of heart disease discovered were already known by virtue of the recently established Mesa County Heart Disease Registry. This registry is kept in the Mesa County Health Department and designed to insure follow-up of those patients supposed to be on a prophylactic regimen against recurrent attacks of rheumatic fever. Another group of cases of heart disease found during the screening program were already known to the children's physicians. However, the majority of the cases of heart disease discovered during the screening program were previously unknown. This information is presented in table 3.

The registry actually is much more adequate than table 3 would indicate. It contained the names of 22 of the 50 children listed as having had rheumatic fever. This incomplete coverage is partly a result of the short time that the registry had been established and partly a result of the reluctance of physicians to fill out report forms. It should be mentioned that three of the children with known congenital heart disease had already had corrective surgery.

The primary reason for collecting figures and recording data was to obtain as good a basis as possible for the estimation of prevalence rates for congenital and rheumatic heart disease in this age group. To have completely reliable figures, one would need a population group large enough to provide at least 50 cases of congenital heart disease and 50 of rheumatic heart disease. Unfortunately, the population being reported is apparently not large enough. However, it is believed the figures obtained should be reported with the caution that larger population studies may report different figures which might be more reliable.

TABLE 3.—*Comparison of Diagnoses with Previous Knowledge of Heart Disease*

		Mesa County Registry			Other Knowledge, No.		
		Listed, No.					
Heart Disease	Total	Correct Diagnosis	Incorrect Diagnosis	Not Listed, No.	Correct Diagnosis	Incorrect Diagnosis	Not Known, No.
Congenital	33	1	0	32	6	5	21
Rheumatic	7	1	0	6	2	0	4
Other	1	0	0	1	0	0	1
ECG abnormality	3	0	0	3	0	0	3
Total	44	2	0	42	8	5	29

The prevalence rate of a condition is defined as the number of cases of that condition known to exist in a given population at any one time. For this particular prevalence ratio, the numerator will be composed only of the 40 cases of congenital and rheumatic heart disease. The electrocardiographic abnormalities are not included, since they do not constitute organic heart defects. The case of cor pulmonale is not included because it is probably a transient condition. In the choice of a denominator for the prevalence estimate, one could use the total population at risk (6,604) and compute a minimum prevalence rate, or one could use only the population examined (6,311) and compute a maximum prevalence rate. Both sets of prevalence rates are presented in tabular form in table 4.

TABLE 4.—*Prevalence Rates, in Percentage, of Organic Heart Disease in Elementary School Children*

Heart Disease	Total Population at Risk (6,604)	Examined Population (6,311)
Organic	0.61	0.63
Congenital	0.50	0.52
Rheumatic	0.11	0.11

It may seem to be excessive detail to present both sets of prevalence figures when they are obviously so close, but prevalence estimates have been made from studies based on examinations of a much smaller percentage of the total population at risk. In such instances the two sets of figures represent two ways of regarding the results; they can be further apart; and the difference becomes more significant. The possible significance of the over-all prevalence rate and the rates for rheumatic and congenital heart disease will be discussed in a later paper.

Functional or innocent heart murmurs in children are a fascinating topic, and there is no completely satisfactory explanation for most of them.[3] As with prevalence rates of heart disease, different studies have shown different percentages of the population with an innocent heart murmur. It is probable that most of the differences of opinion about this problem are due to different definitions of terms and to different levels of significance ascribed to what was heard. For the Mesa County program, it was considered advisable to keep a record of all the murmurs heard and their locations. This information is presented in table 5 for all the children without heart disease.

Grade 1 murmurs are included in the records, although no effort was made to keep track of the loudness of the murmurs because of differences in standards and terminology among the examining physicians. Occasional innocent murmurs were as loud as grade 3 on a 6-grade scale. "Venous hums" were included in the group of murmurs heard at the base of the heart. The subdivision of the locations of innocent heart murmurs shown in table 5 was unsatisfactory, since it was noted during the screening program to be not adequately subdivided as to locations and, in some, for sound quality. Perhaps a mimeographed diagram of the precordium should have been included on the record card. This would have permitted more exact differentiation of the location of the innocent murmurs and would have been worth the effort.

A facet of the innocent heart murmur that could stand further clarification is the quality of the sound. "Vibratory" is the term most commonly accepted in the Rocky Mountain area[4] to describe the sound quality of the classic innocent murmur; this denotes a relatively pure sound accompanied by harmonious overtones. However, these murmurs are often composed of disharmonious overtones, and all are not "vibratory" in quality. Some have a definite blowing quality, others are slightly rough, and others are squeaky. This is really a problem in semantics. Although the pitch of the innocent murmur is usually described as low, this is a characteristic of the innocent murmur that often is not too closely attended. To those of us without a phonocardiogram, pitch may most readily be determined by the relative difference between the sound as heard through the diaphragm of the stethoscope (high-pitched sounds are heard relatively better) and the sound as heard through the bell of the stethoscope (low-pitched sounds are heard relatively better). Although probably many functional heart murmurs are indeed low-pitched, many must be called medium-pitched.

TABLE 5.—*Comparison of Age and Sex with Innocent Heart Murmurs and Their Locations*

		Murmurs,* No.							
Age, Yr.	Sex	None	Base	L.S.B.	L.S.B. and Base	L.S.B. and Apex	W.P.	Total Murmurs	Total
5	M	12	0	9	4	4	3	20	32
	F	23	1	6	1	2	1	11	34
6	M	282	29	76	6	31	15	157	439
	F	290	23	74	9	18	13	137	427
7	M	311	27	103	4	36	16	186	497
	F	340	32	72	7	24	14	149	489
8	M	344	26	101	6	25	11	169	513
	F	380	31	79	12	21	10	153	533
9	M	361	25	90	9	21	18	163	524
	F	354	24	65	6	16	9	120	474
10	M	358	28	109	3	24	14	178	536
	F	319	46	98	14	17	14	189	508
11	M	336	33	73	12	26	9	153	489
	F	307	36	97	9	15	12	169	476
12	M	94	5	34	0	10	2	51	145
	F	54	10	29	2	3	3	47	101
13	M	19	1	3	0	1	2	7	26
	F	13	2	3	0	0	0	5	18
14 or older	M	2	0	3	0	0	0	3	5
	F	2	0	1	0	0	0	1	3
Totals	M	2,119	174	601	44	178	90	1,087	3,206
	F	2,082	205	524	60	116	76	981	3,063
Both sexes		4,201	379	1,125	104	294	116	2,068	6,269

* L.S.B. = left sternal border; W.P. = whole precordium.

The great hallmark of the innocent heart murmur is its variability with respiratory and positional changes. The murmur may completely disappear during a moderately deep, held inspiration, while "organic" murmurs do not. The murmur may be audible when the subject is in the recumbent position and not when he is in the erect position or, rarely, vice versa. The point where the murmur is heard loudest often shifts considerably when the subject's position changes. Exertion may accentuate or diminish the murmur. Anxiety mimics the effects of exertion, especially in children.

Table 5 shows that there are more boys than girls with functional heart murmur. There were also more boys screened than girls. However, among the children 10 and 11 years old, more girls than boys had murmurs. It is doubtful that the totals of each sex in each age group are large enough to be conclusive in this regard. The over-all percentage of innocent heart murmurs heard in normal children in this study (33%) agrees well with percentages found in previous similar studies on Colorado children: 30% of 1,617 elementary school children[2] and 36% of 11,236 sixth graders.[5] This fact would suggest a certain degree of comparability with the previous studies.

No effort was made to obtain statistics on variations in heart sounds heard during the screening program. In particular, the respiratory variation in the splitting of the second heart sound as heard in the second left intercostal space was a closely attended phenomenon during each auscultation. Especially in children, the second heart sound in the "pulmonary area" usually is split during inspiration and single or less widely split during expiration.[6] During this and previous screening activities, it was noted that this split varied in normal children from being only occasionally heard during inspirations to a practically constant wide splitting during expirations. Of course, the loudness of the second sound is of considerable assistance in judging the normality of the respiratory splitting which is significant, since pulmonary hypertension will usually cause a loud and often snapping second heart sound with loss of the respiratory variations in splitting and a fixed reduplication. In addition, a constantly pure second sound in the pulmonary area may be a feature of pulmonary or aortic stenosis, although this has been reported to be an inconstant phenomenon.[7] Inspiratory splitting of the first heart sound along the lower left sternal border and at the apex was another event that could have been recorded. Perhaps another similar study could shed more light on the normal variations and occurrence of heart sounds as well as heart murmurs. This problem is of particular interest because heart sounds are often of more value in identification of heart disease than heart murmurs. Indeed, heart murmurs are usually judged by the accompanying sounds.

It is interesting to note what was advised as to recommendations for the children who were reexamined. This is shown in table 6. The recommendations were made with primary attention to which course of action would be the most practical in a community 260 miles away from where cardiac catheterization could be done. In addition, two of the children with congenital defects were being followed for serious primary mental deficiencies as well, and it was considered that expensive corrective procedures were best deferred in these instances.

Comment

Most physicians work with patients who come or are brought to them with a complaint. In the field of pediatric heart disease this means that, by the time the physician sees the patient, the patient usually has fairly characteristic signs of illness from which a diagnosis may be extracted. As might be expected, a screening program will tend to discover patients in an earlier stage of the progression of their condition. This means that often the diagnostic signs will be more equivocal in the patient with previously unknown heart disease than at a later date when symptoms might have caused him to seek a physician's care. This phenomenon is especially apparent in congenital heart disease wherein there are wide variations in the rate of progression of the condition and its complications, depending on the extent of the defect and on unknown factors in the constitution of the patient. In this study, as in a previous one,[2] relatively mild degrees of congenital defects without functional impairment, such as localized ventricular septal defect (Roger's disease) or some cases of atrial septal defect, pulmonary stenosis, and aortic stenosis, are included as definite congenital heart disease because knowledge at present cannot definitely rule out the possibility that these persons may some day have disability as a result of their defect. This is also the line of reasoning responsible for classifying the case of arachnodactyly as congenital heart disease, even though there is as yet no demonstrable defect. In congenital heart lesions, it is particularly important to discover defects (especially shunts) before irreversible pulmonary hypertension has set in, so that life will actually be prolonged by corrective surgery.

The case of one 7-year-old girl, included in the "normal" category in table 2, may illustrate a phenomenon recently described by Silber,[8] who mentions that viral carditis may produce transient murmurs identical with those of rheumatic heart disease. At the time of the primary screening examination, the girl had had a low-grade fever and wet cough, that had been present for about two weeks, some lassitude, and a grade 3, blowing, high-pitched pansystolic murmur heard all over the precordium, loudest at the apex, radiating to the left axilla, and accompanied by a muffled first heart sound in the "mitral area." Intermittent rhonchi were heard over both lung fields. There was no other history of any other manifestations of rheumatic fever, her sedimentation rate was normal, and her family history was negative. Although this does not rule out the supposed entity of subclinical rheumatic fever, there was no acute episode of rheumatic fever to account for the very definite and previously unheard murmur of mitral insufficiency. Four weeks later, when she was reexamined by the pediatric cardiologist in conjunction with the screening physician, it was readily agreed that the patient had a grade 2, vibratory, low-pitched systolic murmur heard all over the precordium, loudest in the fourth left intercostal space, and not heard in the left axilla. At this time the first heart sound was entirely normal, there was no indication of upper or lower respiratory tract infection, and the heart murmur was judged to be classically innocent. In the interval between the examinations, the patient had been receiving orally one penicillin tablet per day, but no anti-inflammatory drugs, and she had not been kept home from school. Of course the possibility of an endocarditis has not been ruled out, although this is a little remote considering the

TABLE 6.—*Comparison of Diagnostic Categories with Recommendations in Discovered Cases of Heart Disease*

		Other Studies Needed					Surgery			
				Reexamination After						
	Total	None	Cardiac Catheterization	1 Yr.	2 Yr.	5 Yr.	No	Yes	Depending on Result of Cardiac Catheterization	Already Done
Heart disease										
Congenital..	33	8	14		10	1	14	6	10	3
Rheumatic..	7		1	5	1		6		1	
Other.......	1				1		1			
ECG abnormality......	3	3					3			
History of rheumatic fever........	50			1	49		50			
No heart disease......	71	58		1	12		71			
Total.......	165	69	15	7	73	1	145	6	11	3

clinical course. Since a virus or its antibody response was not definitely identified, the case is open to speculation, but the hypothesis of transient viral carditis is interesting and thought-provoking.

The physicians of this Colorado town are, as a group, probably as well-trained and able to diagnose heart disease as any other comparable group in the United States. Thus, the fact that 29 of these 43 cases of heart abnormalities were previously unrecognized is no reflection on the local medical practice. As previously mentioned, most of those children were not having the symptoms or signs of illness that would cause their parents to seek medical attention. In addition, many of the incorrect previous diagnoses mentioned in table 3 had been made by paramedical personnel in the community (who seem interested in heart disease but not as well trained in the subject).

One discouraging facet of this sort of program is that not all the subjects in whom heart disease is discovered will receive the recommended diagnostic studies or corrective operation. In fact, from past experience gleaned from other similar surveys, probably only about one-half of those who have not already had an operation and in whom disease was discovered in this survey will actually receive the benefit of the available therapeutic potential in time to really prolong life to somewhere around the normal expectation. There are many reasons for this, most of them sociological: parental maladjustments, distrust of doctors, financial embarrassment, refusal to accept the free care available, and other factors. Cases of acyanotic congenital heart disease are particularly apt to result this way because the children "don't look sick" to the parents. By the time they do look sick enough, it is often too late in the progression of the disease to obtain a cure by operation; either the patient is too poor a surgical risk, or irreversible pulmonary vascular changes have occurred. This sort of thing is probably more apt to happen in a rural then an urban population.

It is as important to avoid overdiagnosis as underdiagnosis. The production of excessive anxiety concerning the heart should be avoided if possible. That considerable anxiety is generated in the children by such a screening procedure is apparent when one discovers later from teachers and parents what comments the children have made and to what lengths they sometimes go to avoid the screening procedure.

It can be readily seen that the discovery of previously unknown cases of heart disease is a significant event. Children with rheumatic heart disease may be placed on a prophylactic regimen against recurrent attacks of rheumatic fever, and children with congenital heart disease may undergo corrective operation or may be given follow-up examinations until such time as the development of symptoms or signs of dysfunction might make operation desirable. However, the other side of the coin is that there were at least 15 children who were relieved of a false diagnosis of heart disease. This is a minimum figure, since this result was not anticipated and the records kept did not include previous diagnoses on all the normal children. These children were usually on rather severely restricted activity regimens and in some cases were real behavior problems in school and at home, utilizing their supposed heart defect to immunize themselves against punishment. However, it is possible that some of these children received their diagnosis during an episode of illness similar in effect to the one described in the 7-year-old girl with an upper respiratory infection. The possibilities for error make it necessary to examine a child at least twice before making a definite diagnosis of heart disease.

Summary

In a screening program for heart disease in elementary school children, 33 cases of congenital heart disease and 7 of rheumatic heart disease were discovered in a total population of 6,604 children, 95.6% of whom were examined. Other types of heart abnormality were also found. Of the children without heart disease, 33% had innocent heart murmurs.

222 39th Ave., San Mateo, Calif. (Dr. Morton).

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COMPARISON OF THREE METHODS OF SCREENING FOR PEDIATRIC HEART DISEASE

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Three screening methods were compared as to specificity and sensitiveness in the detection of cardiac abnormalities by applying them to each of 5,654 children. The three methods consisted of a single-lead (V_3R) electrocardiogram, a miniature chest roentgenogram, and a limited physical examination. For each method it was possible to define a sensitivity index, a specificity index, and their product, an efficiency index. The V_3R gave a specificity index of 0.190 (ratio of true positive to total positive findings), and of 58 children with abnormal V_3R tracings 44 had normal hearts. The physical examination, used singly, was the most specific and the most sensitive and gave the highest efficiency index, but none of the methods was infallible.

Screening methods for the purpose of detecting heart disease have received extensive evaluation in adults. Screening programs with use of chest x-ray, brief history, limited physical examination, blood pressure recordings, and electrocardiogram singly or in combination have been described.[1] In adults, rheumatic heart disease and hypertensive heart disease are more readily discovered by screening, but arteriosclerotic heart disease (the major problem) is considerably more difficult to detect on a screening basis unless angina pectoris is present or a myocardial infarction has occurred, and even then detection of disease is not easy. It has also been the experience in previous studies that incipient or even frank cor pulmonale in adults is difficult to detect on a screening basis.

However, in children, the problem of screening for heart disease is made easier by the fact that the two commonest types of heart disease, congenital and rheumatic, generally produce specific chamber enlargement, pulmonary vascular changes, or characteristic heart murmurs which produce definite auscultatory electrocardiographic, or radiologic signs.

Increased consciousness of heart disease on the part of the general public, the development of corrective surgery for various types of heart disease, and the development of effective prophylaxis against recurrent attacks of rheumatic fever have made the discovery of heart disease among children a valid community public health activity. This is especially true since most physicians have neither the time nor the desire (and often not the experience) to screen hundreds and sometimes thousands of children to weed out the approximately 0.5 to 1.0% of children who have heart disease and who will benefit from medical attention.

There is a need for more information regarding the sensitivity, specificity, and reliability of the various methods which might be used singly or in combination in screening for pediatric heart disease. Estimates of these must be based on studies of large populations of children in which all have been checked by the best other method in addition to the one being tested. For purposes of statistical validity, it is estimated that the population should be large enough to yield at least 50 cases of heart disease, which would mean that at least 5,000 to 10,000 children should be screened to test any given method.

The only real practical check available to evaluate the various screening methods is the total evaluation, including history, careful physical examination by physicians experienced in cardiac diagnosis, electrocardiogram, x-ray, and, at times, selected physiological tests. It becomes apparent that the problem of evaluation of a single diagnostic test is a difficult process. The primary purpose of this paper is to present the information obtained from three screening methods used simultaneously on the same group of grade school children.

Method

Over a period of two school years in two western Colorado communities, a total of 5,654 grade school children were examined by single-lead electrocardiogram, miniature chest x-ray, and limited physical examination. A total of 7,928 children were examined by at least one method, but only 5,654 were subjected to all three screening methods. The prevalence rates noted for heart disease and innocent

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With the Heart Disease Control Program, U. S. Public Health Service, assigned to the Colorado State Department of Public Health (Dr. Morton); Chief of Cardiology, National Jewish Hospital (Dr. Hoffman); Executive Director, Colorado State Department of Public Health (Dr. Cleere); and acting head of the Department of Preventive Medicine, University of Colorado Medical Center (Dr. Dodge). Dr. Morton is now a resident in medicine at San Mateo County Community Hospital, San Mateo, Calif. Dr. Dodge is now Professor of Epidemiology, University of Michigan School of Public Health, Ann Arbor, Mich.

heart murmurs have been reported elsewhere,[2] and this report will concentrate on the comparison of sensitivity and specificity of the three methods used.

The primary physical examination was performed by selected physicians experienced in cardiac diagnosis; it consisted of inspection of the jugular venous pulses, palpation of the radial and femoral arterial pulses, inspection and palpation of the chest, and auscultation of the heart with the child in several positions and with attention to respiratory variations in heart sounds. Blood pressure recordings from arms and legs were obtained when indicated by heart sounds or arterial pulse characteristics.

TABLE 1.—*Comparison of Processing Rates for Three Screening Methods for Heart Disease*

Primary Screening Test	Personnel Required	Children Examined per School Day, No.	Results Read per Hr., No.
Physical examination (1 team of 2 M.D.'s)	2 physicians, 1 nurse, 2 PTA mothers	300-400	Immediate
ECG, V_3R lead (1 machine)	1 trained nurse or technician, 2 PTA mothers	200-300	500-600
70-mm. chest x-ray (mobile unit)	2 technicians and 2 PTA mothers or 1 technician and 3 PTA mothers	500-600	400-500

The single V_3R lead of the electrocardiogram was used as a screening tool because a large proportion of the congenital heart defects found in this age group are conditions associated with right ventricular hypertrophy, most readily detected by right precordial leads. Two criteria for this abnormality were used: (1) ratio of R wave to S wave greater than unity and (2) ventricular activation time (from onset of QRS complex to peak of tallest R wave) of 0.04 seconds or longer. If both criteria were present, the tracing was considered abnormal. If only one criterion was present, the finding was considered borderline. The tracings were obtained by registered nurses who were trained for this task, and they were assisted by mothers from the Parent-Teacher Association. Alcohol sponges were used in place of electrode paste to save time.

The state mobile x-ray unit, ordinarily devoted to screening for tuberculosis, was used to obtain 70-mm. chest x-rays. The x-rays obtained in the heart disease screening program were also examined for tuberculosis, and as a result 10 children were suspected of having the latter disease. Children were noted by the technicians to require more effort to x-ray than adults, and the smallest children stood on various sized boxes in order to reach the screen. Since the screening procedures were organized to be performed in rapid succession on the same children, it was necessary to know the rate at which children could be processed. Table 1 presents the maximum performance rates for the three methods. The PTA mothers listed under personnel are used for dressing and undressing children, keeping noise down to a reasonable level, seeing that no children are overlooked, and similar needs. Usually the children are brought to the examining site by class, and the teachers are also present.

Actual organization of screening schedules and auxiliary personnel was done by the public health and school nurses from the local health departments. One or two nurses were always present during the screening procedure. The entire program was coordinated by the Heart Disease Control Program of the Colorado State Department of Public Health and financed by the Colorado Heart Association. Screening physicians were provided largely from Denver, although there was some participation by interested physicians in each community.

As a result of the primary screening phase of the program, any child screened out by any of the three methods was reexamined by a pediatric cardiologist who utilized complete history, physical examination, electrocardiogram, full-size chest x-rays, fluoroscopy, and, at times, such physiological procedure as heart catheterization. The parents were told of the findings on the spot, and, in addition, letters were mailed to family physicians describing the findings, the probable diagnosis, and any further recommendations.

Results

Table 2 shows the age and sex distribution of the children screened for heart disease by all three methods. From this table, it may be seen that a representative population (with respect to age and sex distribution) of grade school children was screened.

Accumulating the results of all three screening methods, this population of 5,654 children included 36 with congenital heart disease, 5 with rheumatic heart disease, 1 with "other" heart disease (cor pulmonale), and three with electrocardiographic abnormality without organic heart disease; 5,609 children were normal.

Since the V_3R lead was used to detect right ventricular hypertrophy only, the children were divided into those with this condition and all others. The child with "other" heart disease happened to have right ventricular hypertrophy. The three cases of electrocardiographic abnormality without organic heart disease consisted of two of anomalous muscle bundle between atrium and ventricle (Wolff-Parkinson-White syndrome) and one of isolated, complete, right bundle-branch block. The children with rheumatic heart disease all had mitral valve involvement only. The cases of congenital heart disease

TABLE 2.—*Comparison of Age and Sex of Children Screened for Heart Disease*

	Age, Yr.									
Sex	5	6	7	8	9	10	11	12	13+	Total
Male, no. ...	2	468	477	465	498	455	403	110	16	2,894
Female, no. .	4	438	477	481	455	417	384	90	14	2,760
Total	6	906	954	946	953	872	787	200	30	5,654

consisted of 10 of atrial septal defect, 5 of ventricular septal defect, 5 of aortic stenosis, 5 of pulmonary stenosis, 3 of patent ductus arteriosus, 2 of coarctation of the aorta, 1 of arachnodactyly (Marfan's syndrome), 1 of dextrocardia, 1 of tetralogy of Fallot, and 3 of congenital heart disease, type unknown.

When considering the number of different screening methods, it is helpful to consider the specificity of the tests for a condition and the sensitivity of the tests in detecting the condition. These terms give a numerical measure of the tests. Thus, the following definitions of terms are in order: 1. Specificity. A test is wholly specific when the result is positive only in the presence of the condition for which the test is made. The measure of specificity is the ratio of true positive tests to total positive tests. 2. Sensitivity. A test is wholly sensitive when the result is invariably positive in the presence of the condition for which the test is made. The measure of sensitivity is the ratio of true positive tests to the total number of patients having the condition for which the test is made. 3. Efficiency. In order to have some expression which will combine specificity and sensitivity, an index of efficiency is calculated by multiplying the ratios of specificity and sensitivity.

A screening test with a relatively high sensitivity may have a relatively low specificity and vice versa. By inspection of table 3, it will be seen that all the screening methods missed cases of heart disease (false-negative results) and all gave a certain proportion of false-positive results. It is helpful to assemble these figures in another table (table 4) for comparison.

Table 3.—*Comparison of Diagnostic Categories with Results of Three Methods of Screening for Heart Disease*

		Results, No.						
		Physical Examination		ECG, V₃R Lead			Chest X-ray, 70 Mm.	
Diagnosis	Total	Positive	Negative	Abnormal	Borderline	Normal	Positive	Negative
Congenital heart disease								
Right ventricular hypertrophy	13	10	3	11	1	1	7	6
Other	23	20	3	0	5	18	5	18
Rheumatic heart disease	5	5	0	0	0	5	3	2
Other heart disease (cor pulmonale)	1	0	1	0	1	0	0	1
ECG abnormality	3	0	3	3	0	0	0	3
Normal	5,609	72	5,537	44	437	5,128	41	5,568
Total	5,654	107	5,547	58	444	5,152	56	5,598

It is interesting to note that seven cases of heart disease would have been missed by use of the physical examination alone. In judging the V_3R lead, only the "abnormal" category was considered as positive in computing the specificity, and only the cases of right ventricular hypertrophy were considered in computing the sensitivity. As has probably been noticed, table 4 was computed on the assumption that the screening program discovered all the cases of heart disease within the population of 5,654 children. This is only an assumption, because cases could have been missed even with the simultaneous use of three screening tests. The only way to gain a more reliable foundation for this sort of work would be to examine every one of a population of several thousand children at a diagnostic center where they would receive a complete diagnostic study, including fluoroscopy.

Table 4.—*Comparison of Specificity, Sensitivity, and Efficiency of Three Screening Methods, Used Alone and in Combination*

	Specificity†		Sensitivity‡		
Method*	Ratio	Quotient	Ratio	Quotient	Index of Efficiency§
Physical examination	35:107	0.327	35:42	0.833	0.272
ECG, V₃R lead	11:58	0.190	11:14	0.786	0.149
Chest x-ray, 70 mm.	15:56	0.268	15:42	0.357	0.096
Physical examination plus ECG	37:150	0.247	37:42	0.881	0.218
Physical examination plus x-ray	37:152	0.243	37:42	0.881	0.214
Chest x-ray plus ECG	20:107	0.187	20:42	0.476	0.093

* All methods except that with ECG alone (for right ventricular hypertrophy) computed for all heart disease.

† Ratio of true positive tests to total positive tests.

‡ Ratio of true positive tests to total number of subjects with condition for which test is done.

§ Ratios for specificity and sensitivity multiplied.

Of the three screening methods used singly, the physical examination was the most specific, although all methods were fairly close in this respect and produced many false-positive results. The V_3R lead was the least specific, even though it was only judged in the detection of right ventricular hypertrophy. The physical examination was also the most sensitive, with the V_3R lead a close second (only in the detection of right ventricular hypertrophy) and the 70-mm. chest x-ray a poor third. Thus, the physical examination seemed to be the most efficient screening method.

Inspection of the tabular comparison between the various combinations of screening methods (table 4) shows that, although use of the physical examination in conjunction with either the V_3R lead or the 70-mm. chest x-ray will increase the sensitivity of the screening program, the specificity would then fall below the value obtained when only the physical examination is used as a screening method. Of course, the combination of all three screening methods used simultaneously is even more sensitive but less specific than the physical examination used alone. However, there is nothing against which to measure the over-all sensitivity of the entire screening program in this study.

Comment

It must be remembered that these screening programs were conducted afresh in each community and that, if this program were set up on a continuing basis with the community physicians gaining experience in screening for heart disease each year, the values presented for specificity, sensitivity, and efficiency of the screening program should rise. Also, it would certainly be much more advantageous in respect to time and finances to screen for heart disease with use of only one screening method instead of three. At the most, two methods might be used simultaneously.

The V_3R lead was fairly sensitive in the detection of right ventricular hypertrophy, and considerable moral support was given to the screening physicians when the tracing was taken just before the physical examination and attached to the child's record card. It must be pointed out that the electrocardiographic criteria used herein for the diagnosis of right ventricular hypertrophy were limited by the technique, in that such patterns as deep S waves in the left precordial leads or shift in precordial transitional zone to the left could not be used to make this diagnosis. Had complete electrocardiographic tracings been obtained on each of these children and read for right ventricular hypertrophy, the screening method would probably have been more sensitive but would have lost a good deal of specificity. It should be emphasized that, of the 58 children with abnormal V_3R tracings, as judged by rather strict standards, only 11 had right ventricular hypertrophy, 3 had electrocardiographic abnormalities, and 44 had normal hearts. The 44 normal children with electrocardiographic evidence of right ventricular hypertrophy should cause one to reflect that the electrocardiogram is an ancillary and not a primary diagnostic tool. However, it would seem to be an advantage to have electrocardiographic assistance in the diagnosis of conditions which might cause left ventricular hypertrophy or combined ventricular hypertrophy. A complete electrocardiogram would probably complicate the record handling and interpretation procedures too much to be of that much additional value. However, since the child is already "wired" for a chest lead, perhaps one or maybe two additional leads could be recorded and judged by definite criteria without loss of the relative simplicity of the procedure.

The chest x-ray is not a sensitive tool with which to detect heart disease, especially in children, most of whom are in an early stage of their disease. It is certainly an excellent means, however, of following changes in heart size and configuration and in pulmonary vascularity in patients whose heart disease is already known. X-rays are also invaluable in making a diagnosis of heart disease. The screening efficiency of the x-ray was decreased by the fact that there is a wide range of normal appearance of the heart contour. This, coupled with the fact that many of the subjects screened had no gross cardiac enlargement, made the method less desirable for this purpose in this age group. In view of the cost and size of x-ray equipment, the chest x-ray probably does not have as much developmental potential as a mass screening tool as other methods.

This study, with simultaneous use of three screening procedures, has established one fact: no screening method is infallible. Even in the physical examination, when performed by experts, heart disease can be overlooked in an age group in which it has previously been thought that heart disease should not be missed. This has a bearing on past studies of prevalence rates of heart disease in this age group, which have usually been based on the physical examination. It means that, if the studies were performed on large enough groups of children (over 5,000), the prevalence rates offered probably erred on the low side of the true prevalence rates.

Recently, several investigators have been developing the phonocardiogram with heart sound recordings on hi-fi tape as a mass screening tool for discovering heart disease among children. The phonocardiogram operated by a technician would save physicians' time and make possible the screening of a large number of children with minimum expense. It must be remembered that the phonocardiogram as used in this fashion would be an ancillary tool, as are the electrocardiogram and the chest x-ray, and it should not be expected to measure up to the results of a screening program with trained physicians who use their hands and eyes in addition to their ears. This is merely to caution against overenthusiasm for a new tool and not to detract from the many obvious advantages of working with a phonocardiogram in this fashion.

The population of 5,654 children in this study cannot be used in computing prevalence rates of heart disease, since it was arbitrarily selected from a larger group of 7,928 children screened. The group discussed in this paper was selected solely on the basis of having had all three screening procedures performed.

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INTRAVENOUS USE OF OXYTOCIN (PITOCIN) FOR INDUCTION OF LABOR

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The extent to which oxytocin is being used to initiate or stimulate uterine contractions in labor was investigated by analyzing certain information on birth and fetal death certificates in New York City. Of 165,150 live births in 1955, 7,694 (4.7%) were induced with intravenously given oxytocin. In 1956 the over-all reported incidence rose to 5.0%. Three case-histories are given to illustrate the irrational use of this drug. The data showed that its use was influenced by the season of the year and by the socioeconomic status of the patient and that in cesarean sections and breech deliveries the prior use of oxytocin increased the infant mortality.

Posterior pituitary products, administered intramuscularly, were used in obstetrics for many decades for the induction and/or stimulation of labor. A new modality, oxytocin (Pitocin), diluted for intravenous use, was first suggested for stimulation and induction of labor by Page[1] in 1943. His report was followed in 1949-1950 by the clinical reports of Theobald and others[2] and Hellman[3] on dilute oxytocin in 5% glucose solution (1:5,000 to 1:7,000), given intravenously. These reports initiated the widespread use of oxytocin for the induction and stimulation of labor. An ever-increasing trend in this usage is attested by subsequent reports in the literature.[4]

Many questions, such as the following, need to be raised regarding the possible deleterious effects of intravenously given oxytocin. 1. Does it increase the incidence of ruptured uterus? 2. Does it increase the incidence of premature separation of the placenta? 3. Does it increase uterine hemorrhage? 4. Does it increase the incidence of prematurity? 5. Does it increase perinatal mortality? 6. Is it harmful in a breech presentation? 7. Is the infant unduly traumatized? 8. Does it produce fetal anoxia with resultant central nervous system damage that may not be ascertained until years later?

Published studies[5] on intravenously given oxytocin have been confined to an individual hospital or group of hospitals where careful supervision usually prevails. These sources indicate that with proper control this method does not significantly increase the hazard to mother or infant. In an effort to determine the extent of usage and to obtain additional information about the questions raised, this present study was initiated.

Method of Study

This report is based on an analysis of birth and fetal death certificates from New York City for 1955-1956 (see figure). These certificates request the following information: 1. Was induction attempted? 2. Indication? 3. Method of induction? 4. Successful? ("Successful" is interpreted as the initiation of active labor resulting in birth per vaginam.) These items were coded and punched on I. B. M. cards. The coding was set up as shown in table 1.

For the purpose of this study, all certificates coded 4, 5, or 6, which refer to the induction of labor with oxytocin, were included, and the tabulations were limited to these. If oxytocin was stated to be used for "stimulation of labor," then codes 4, 5, or 6 were not utilized and these cases were not included. Information regarding acceleration (or stimulation) of labor is not available from the birth certificate. Failure to answer one or more of the questions on the birth certificate regarding the use of intravenously given oxytocin is recognized as a limitation in this analysis. Many cases of induction are categorized as resulting from "stimulation," and, therefore, the actual incidence is under-reported. Information and correlations were obtained which are of interest and which may serve to stimulate further clinical studies relating to the use of intravenously given oxytocin.

Additional information was obtained from a questionnaire sent to all the directors of obstetric services of hospitals in New York City. This requested information on live births and fetal deaths occurring on the private and ward services, with regard to the use of intravenously given oxytocin for the stimulation and induction of labor. A response was obtained from 79 hospitals, for 1955, with a total of 128,324 live births. These included 49 voluntary, 16 proprietary, and 14 municipal hospitals. A similar questionnaire was sent for the year 1956, was completed by 83 hospitals, and resulted in information on 136,451 live births.

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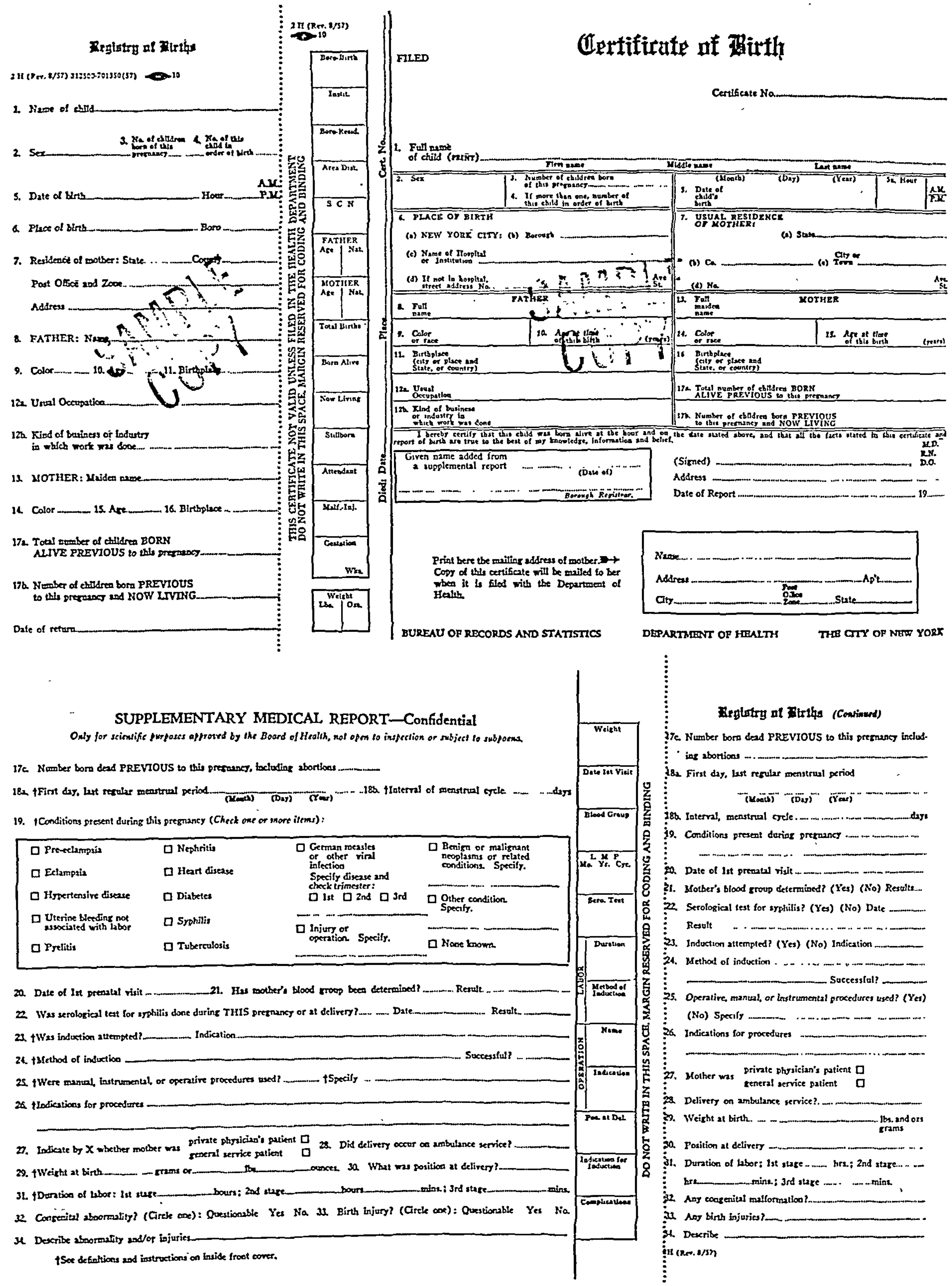

2 H (Rev. 8/57) 10

Registry of Births

2 H (Rev. 8/57) 312503-701350(57) 10

1. Name of child
2. Sex 3. No. of children born of this pregnancy 4. No. of this child in order of birth
5. Date of birth Hour A.M. P.M.
6. Place of birth Boro
7. Residence of mother: State County
Post Office and Zone
Address
8. FATHER: Name
9. Color 10. Age 11. Birthplace
12a. Usual Occupation
12b. Kind of business or industry in which work was done
13. MOTHER: Maiden name
14. Color 15. Age 16. Birthplace
17a. Total number of children BORN ALIVE PREVIOUS to this pregnancy
17b. Number of children born PREVIOUS to this pregnancy and NOW LIVING
Date of return

THIS CERTIFICATE NOT VALID UNLESS FILED IN THE HEALTH DEPARTMENT
DO NOT WRITE IN THIS SPACE, MARGIN RESERVED FOR CODING AND BINDING

Boro-Birth
Instit.
Boro-Resid.
Area Dist.
S C N
FATHER Age Nat.
MOTHER Age Nat.
Total Births
Born Alive
Now Living
Stillborn
Attendant
Malf.-Inj.
Gestation Wks.
Weight Lbs. Ozs.

Cert. No.
Place
Died: Date

FILED

Certificate of Birth

Certificate No.

1. Full name of child (PRINT) First name Middle name Last name
2. Sex
3. Number of children born of this pregnancy
4. If more than one, number of this child in order of birth
5. Date of child's birth (Month) (Day) (Year) 5a. Hour A.M. P.M.
6. PLACE OF BIRTH
(a) NEW YORK CITY: (b) Borough
(c) Name of Hospital or Institution
(d) If not in hospital, street address No. Ave St.
7. USUAL RESIDENCE OF MOTHER:
(a) State
(b) Co. (c) City or Town
(d) No. Ave. St.

FATHER
8. Full name
9. Color or race
10. Age at time of this birth (years)
11. Birthplace (city or place and State, or country)
12a. Usual Occupation
12b. Kind of business or industry in which work was done

MOTHER
13. Full maiden name
14. Color or race
15. Age at time of this birth (years)
16. Birthplace (city or place and State, or country)
17a. Total number of children BORN ALIVE PREVIOUS to this pregnancy
17b. Number of children born PREVIOUS to this pregnancy and NOW LIVING

I hereby certify that this child was born alive at the hour and on the date stated above, and that all the facts stated in this certificate and report of birth are true to the best of my knowledge, information and belief.

Given name added from a supplemental report (Date of)
Borough Registrar.

(Signed) M.D. R.N. D.O.
Address
Date of Report 19

Print here the mailing address of mother. Copy of this certificate will be mailed to her when it is filed with the Department of Health.

Name
Address Ap't
City Post Office Zone State

BUREAU OF RECORDS AND STATISTICS DEPARTMENT OF HEALTH THE CITY OF NEW YORK

SUPPLEMENTARY MEDICAL REPORT—Confidential

Only for scientific purposes approved by the Board of Health, not open to inspection or subject to subpoena.

17c. Number born dead PREVIOUS to this pregnancy, including abortions
18a. †First day, last regular menstrual period (Month) (Day) (Year) 18b. †Interval of menstrual cycle days
19. †Conditions present during this pregnancy (*Check one or more items*):

- ☐ Pre-eclampsia
- ☐ Eclampsia
- ☐ Hypertensive disease
- ☐ Uterine bleeding not associated with labor
- ☐ Pyelitis
- ☐ Nephritis
- ☐ Heart disease
- ☐ Diabetes
- ☐ *Syphilis*
- ☐ Tuberculosis
- ☐ German measles or other viral infection. Specify disease and *check trimester*: ☐ 1st ☐ 2nd ☐ 3rd
- ☐ Injury or operation. Specify.
- ☐ Benign or malignant neoplasms or related conditions. Specify.
- ☐ Other condition. Specify.
- ☐ None known.

20. Date of 1st prenatal visit 21. Has mother's blood group been determined? Result
22. Was serological test for syphilis done during THIS pregnancy or at delivery? Date Result
23. †Was induction attempted? Indication
24. †Method of induction Successful?
25. †Were manual, instrumental, or operative procedures used? †Specify
26. †Indications for procedures
27. Indicate by X whether mother was private physician's patient ☐ general service patient ☐ 28. Did delivery occur on ambulance service?
29. †Weight at birth grams or lbs. ounces. 30. What was position at delivery?
31. †Duration of labor: 1st stage hours; 2nd stage hours mins.; 3rd stage mins.
32. Congenital abnormality? (Circle one): Questionable Yes No. 33. Birth injury? (Circle one): Questionable Yes No.
34. Describe abnormality and/or injuries

†See definitions and instructions on inside front cover.

Weight
Date 1st Visit
Blood Group
L M P Mo. Yr. Cyc.
Sero. Test
LABOR Duration
LABOR Method of Induction
OPERATION Name
OPERATION Indication
Pos. at Del.
Indication for Induction
Complications

DO NOT WRITE IN THIS SPACE, MARGIN RESERVED FOR CODING AND BINDING

Registry of Births *(Continued)*

17c. Number born dead PREVIOUS to this pregnancy including abortions
18a. First day, last regular menstrual period (Month) (Day) (Year)
18b. Interval, menstrual cycle days
19. Conditions present during pregnancy
20. Date of 1st prenatal visit
21. Mother's blood group determined? (Yes) (No) Results
22. Serological test for syphilis? (Yes) (No) Date
Result
23. Induction attempted? (Yes) (No) Indication
24. Method of induction
Successful?
25. *Operative, manual, or instrumental procedures used?* (Yes) (No) Specify
26. Indications for procedures
27. Mother was private physician's patient ☐ general service patient ☐
28. Delivery on ambulance service?
29. Weight at birth lbs. and ozs grams
30. Position at delivery
31. Duration of labor; 1st stage hrs.; 2nd stage hrs. mins.; 3rd stage mins.
32. Any congenital malformation?
33. Any birth injuries?
34. Describe

2H (Rev. 8/57)

Certificate of birth, used in New York City, showing, front, *above*, and back, *below*.

Results

Frequency of Inductions.—Of 165,150 live births in New York City in 1955, 7,694 (4.7%) were induced with intravenously given oxytocin. In 1956 the over-all reported incidence rose to 5.0%. In 1955, of 103,791 births on the private service, 6,890 (6.6%) were induced with oxytocin; of 58,991 births on ward services, 804 (1.4%) were induced. In 1956 an increase in utilization of oxytocin occurred in both private (7%) and ward services (1.7%). These data would indicate that oxytocin is used approximately five times more frequently on private than on ward services. A variation is noted among private patients, depending on whether they are delivered in voluntary or proprietary hospitals. Oxytocin is used two and one-half times more frequently on the private services of voluntary hospitals than on those of proprietary hospitals.

TABLE 1.—*Coding Methods Used for Data Taken from Birth and Fetal Death Certificates*

Code No.	Indications for Induction of Labor	Method of Induction of Labor
0	Not induced	Not induced
1	Elective	Other than oxytocin, successful
2	Therapeutic (including postmaturity, rupture of membranes, erythroblastosis, Rh—, premature separation of placenta, placenta previa, abruptio placentae, and ablatio placentae)	Other than oxytocin, not successful
3	Dead baby—no fetal heartbeat	Other than oxytocin, success not stated
4	Other (including nephritis, heart disease, diabetes, syphilis, tuberculosis, benign neoplasms, malignant neoplasms, and hypertension)	Posterior pituitary injection (Pituitrin) and/or oxytocin, successful
5	Uterine bleeding	Posterior pituitary injection and/or oxytocin, not successful
6	Toxemia (eclampsia and preeclampsia)	Posterior pituitary injection and/or oxytocin, success not stated
7	Indications not stated	Attempted induction, method not stated
8	Not stated whether induced	Not stated whether induced

Indications for Induction of Labor.—Elective induction constitutes approximately half of all inductions in 1955-1956. Of the 7,694 inductions in 1955, 3,688 were elective; of these, 3,548 (96%) were in private patients (table 2). Of the 6,890 inductions on the private service in 1955, 3,548 (51.5%) were for elective reasons, whereas of 804 on ward services, only 140 (17.4%) were elective. It would appear that on ward services oxytocin is used mainly where a therapeutic indication exists, whereas on private service the indication is chiefly elective. It is of interest that in 1956 an increased trend for elective induction is noted even on the ward services.

Use of Oxytocin by Type of Hospital.—Among the 100 hospitals (excluding two federal hospitals) with maternity services in New York City, three categories exist. They are (1) proprietary hospitals—privately owned and services limited entirely to private patients, (2) municipal hospitals—under the jurisdiction of the department of hospitals and limited to ward patients, and (3) voluntary hospitals—having both ward and private patients in varying proportions, depending on the given hospitals. A wide range in the use of intravenously given oxytocin was observed among the hospitals, in 1955, varying from a high of 29.9% to a low of 0.1% (table 3). In 1956 the hospital previously exhibiting the greatest use of this drug showed an even greater rise—to 54.2%.

Results of Questionnaire.—Oxytocin, for both induction and stimulation of labor, was used in 14.0% of 128,324 live births in 1955; 6.4% of live births were induced with intravenously given oxytocin, and 7.6% of live births occurred after its use for the acceleration of labor (table 4). The data obtained in 1956 showed little change from those of 1955. For both years combined, induction on the private service was recorded for 9.1% of the births as compared with 1.8% for the ward service. Stimulation on the private service was noted in 11.9% of cases as compared with 3.2% on the ward service. Induction was used almost twice as frequently on ward services of voluntary hospitals as on ward services of municipal hospitals. To a lesser degree the same trend is shown for stimulation. Among private patients, induction was used more than two and one-half times as frequently in voluntary hospitals as in proprietary hospitals. Again, to a lesser degree, the same trend is shown for stimulation.

TABLE 2.—*Indications for Induction of Labor for Live Births, by Type of Service, New York City, 1955 and 1956*

	1955						1956					
	Total		Private Service		Ward Service		Total		Private Service		Ward Service	
Indication for Induction	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Elective	3,688	47.9	3,548	51.5	140	17.4	4,015	48.7	3,776	52.5	239	22.5
Therapeutic	1,910	24.8	1,702	24.7	208	25.9	1,721	20.9	1,525	21.2	196	18.5
No fetal heartbeat	1	0.0	1	0.0	...	...	...	...	...	...	...	...
Other	181	2.4	139	2.0	42	5.2	210	2.5	160	2.2	50	4.7
Uterine bleeding	82	1.1	58	0.9	24	3.0	94	1.1	79	1.1	15	1.4
Toxemia	602	7.8	443	6.4	159	19.8	472	5.7	331	4.6	141	13.3
Indications not stated	1,230	16.0	999	14.5	231	28.7	1,737	21.1	1,317	18.4	420	39.6
Total	7,694	100.0	6,890	100.0	804	100.0	8,249	100.0	7,188	100.0	1,061	100.0

Seasonal Variation.—Analysis of births after induction by oxytocin revealed a pattern of seasonal variation which was in marked contrast to that exhibited by all live births in New York City. Over a period of years no significant variation in number of births has been found to exist for New York City by month (table 5).

In 1955, peak months for births after induction were observed for July, August, and December. Similar peaks occurred (with the addition of June) in 1956. These rates were significantly higher than those prevailing during the remaining months. The rises were primarily a reflection of usage on private services. By contrast, on the ward service, where the indication is chiefly therapeutic, a plateau is noted. Significantly, in the elective group, the monthly peaks coincided with the over-all use on private service. It would appear that there is a relationship between peak periods of usage and vacation months (table 5).

TABLE 3.—*Percentage of Live Births Induced by Use of Oxytocin, by Type of Hospital, New York City, 1955, 1956*

Live Births, Induced, %	1955				1956			
		Type of Hospital				Type of Hospital		
	Total	Voluntary	Proprietary	Municipal	Total	Voluntary	Proprietary	Municipal
0.1-1.0......	16	6	4	6	14	5	2	7
1.1-2.0......	21	10	6	5	12	3	5	4
2.1-3.0......	10	5	4	1	12	7	5	..
3.1-4.0......	12	5	6	1	7	2	5	..
4.1-5.0......	9	5	4	..	12	8	4	..
5.1-6.0......	10	9	1	..	8	6	2	..
6.1-7.0......	2	2	..	..	5	4	..	1
7.1-8.0......	2	2	..	..	6	6	..	..
8.1-9.0......	4	4	..	..	6	5	..	1
9.1-10	3	3	..	..	1	1	..	..
10.1 & over	11	10	1	..	12	11	1	..
Total..	100	61	26	13	95	58	24	13

Use of Oxytocin in Relation to Age and Parity of Mother.—In New York City, 34% of all live births are to primiparas and 32% to secundiparas. For live births occurring after oxytocin induction, the highest percentage is observed in the secundipara and next in the primipara. A significant observation was made that in 1956 there was an increased use of oxytocin for induction among mothers with a parity of three or more. The age distribution of the mothers in the group given oxytocin approximates the age distribution of mothers for all live births in New York City.

TABLE 4.—*Results on Questionnaire on Use of Oxytocin for Induction and Stimulation of Labor, New York City, 1955 and 1956*

Type of Hospital	Hospitals, No.	Live Births			Induction of Labor			Stimulation of Labor		
		Total	Private Service	Ward Service	Total	Private Service	Ward Service	Total	Private Service	Ward Service
1955										
Voluntary	49	78,327	54,836	23,491	6,895	6,444	451	7,681	6,933	748
Proprietary	16	20,896	20,896	...	833	833	...	1,383	1,383	...
Municipal	14	29,101	207	28,894	469	19	450	715	48	667
Total	79	128,324	75,939	52,385	8,197	7,296	901	9,779	8,364	1,415
1956										
Voluntary	51	81,270	57,539	23,731	6,648	6,025	623	9,582	8,502	1,080
Proprietary	18	24,667	24,661	6	1,134	1,122	12	1,942	1,917	25
Municipal	14	30,514	261	30,253	352	5	347	908	46	862
Total	83	136,451	82,461	53,990	8,134	7,152	982	12,432	10,465	1,967

Conditions Present During Pregnancy.—On the live birth certificates for 1955 the check list indicated at least one or more conditions present during pregnancy in 8% of the cases. In the group of live births where oxytocin was used for induction, one or more conditions were checked in 15%. The higher frequency of "conditions" is as expected, since intravenously given oxytocin is administered for therapeutic as well as elective indications. Preeclampsia and eclampsia were leading conditions noted, with an incidence of 44.5% for both services combined; incidence in private service was 39.3% and in ward service 57.6% (table 6). The higher incidence of preeclampsia and eclampsia on the ward service is not unexpected. Hypertensive disease, heart disease, and neoplasms showed a higher incidence in patients on the private services than on the ward services.

Mode of Delivery.—In patients in whom induction by use of oxytocin was utilized, the percentage of spontaneous deliveries was significantly lower than in those not induced. Conversely, the percentage of forceps deliveries in the induced group was higher for both private and ward services than in those not induced. The higher percentage of forceps deliveries in those induced is to be expected, since oxytocin was used for the purpose of expediting delivery, for either elective or therapeutic reasons (table 7).

The percentage of breech deliveries induced by oxytocin on the private service was lower than that for the noninduced, whereas on the ward service the percentage of breech deliveries in the induced group was not significantly different from that of the noninduced. These differences observed are as anticipated, since in the private service induction is largely done for elective reasons and, therefore, a minimum of breech deliveries would be included.

On the private service, the percentage of cesarean sections in the induced group was much lower than in those not induced. For 1955, the incidence of cesarean section was 2.2% in the induced group as compared with 6.2% for those not so induced. In 1956 a similar relationship is noted (1.9% as compared with 6.1%). This finding also is as expected, since the indication for induction is primarily elective for private patients. By contrast, on the ward service, the percentage of cesarean section is higher in the induced group. This is another reflection of the relatively greater use of oxytocin for therapeutic indications among ward patients.

In 1955-1956, cesarean sections were performed on 372 patients who received oxytocin for induction. Seventy-eight percent of the sections (290) were performed on private patients. In 16.6% (62) of the 372 sections the indication for induction was stated as elective.

In analyzing the data on the group delivered by cesarean section after induction, there were 47 cesarean sections performed for fetal distress. Seven of these patients had received oxytocin on an elective basis. One may draw the inference that fetal distress followed the use of oxytocin, necessitating the section. Of the 98 sections performed for cephalopelvic disproportion, 23 were stated to have been induced electively. These were most likely unrecognized cases of disproportion. In 38 of the 98 cases of cephalopelvic disproportion, it was stated that induction had been used for therapeutic reasons. In these cases it is difficult to reconcile the use of oxytocin in the face of recognized disproportion.

Table 5.—*Live Births Induced by Oxytocin, by Month of Delivery and Type of Service, New York City*

Month of Delivery	Induced Deliveries, No.			Induced Deliveries, %			Elective Inductions	
	Total	Private Service	Ward Service	Total	Private Service	Ward Service	No.	%
1955								
January	476	422	54	3.8	5.4	1.2	159	1.2
February	521	461	60	4.2	5.8	1.3	199	1.6
March	558	487	71	3.9	5.2	1.4	227	1.6
April	637	567	70	4.7	6.3	1.5	287	2.1
May	637	580	57	4.5	6.2	1.2	289	2.0
June	658	607	51	4.7	6.8	1.0	337	2.4
July	726	655	71	5.4	7.7	1.5	362	2.6
August	792	719	73	5.6	8.4	1.3	418	3.0
September	605	527	78	4.4	6.1	1.5	317	2.3
October	639	565	74	4.7	6.6	1.5	309	2.2
November	668	586	82	5.0	6.9	1.7	355	2.7
December	777	714	63	5.8	8.2	1.3	429	3.2
Total	7,694	6.890	804	4.7	6.6	1.4	3,688	2.2
1956								
January	542	475	67	4.0	5.8	1.3	250	1.9
February	592	510	82	4.5	6.2	1.7	293	2.2
March	715	624	91	5.1	7.1	1.9	331	2.4
April	609	544	65	4.9	6.9	1.5	287	2.3
May	663	591	72	5.1	7.1	1.5	305	2.3
June	713	632	81	5.2	7.4	1.7	350	2.5
July	795	701	94	5.4	7.8	1.7	418	2.8
August	757	664	93	5.2	7.2	1.6	404	2.7
September	666	561	105	4.6	7.1	2.1	292	2.0
October	696	597	99	4.8	6.3	1.8	332	2.3
November	653	559	94	4.9	6.5	1.9	331	2.5
December	848	730	118	6.1	8.7	2.4	422	3.0
Total	8,249	7,188	1,061	5.0	7.0	1.7	4,015	2.4

Seven mothers in this group had had previous cesarean sections. This raises the question as to why oxytocin was used at all in this group, since the risk of uterine rupture is acknowledged to be greater in such cases. Eight elderly primiparas (over 35 years of age) were subjected to induction before cesarean section.

Successful Use of Oxytocin.—A definition for successful does not appear in the instructions given for filling out birth certificates. It is understood as meaning the induction of active labor resulting in birth per vaginam. Of the live births induced by use of oxytocin in 1955 and 1956, 80.6% were classified as successful, 2.8% unsuccessful, and 16.6% in neither category.

Table 6.—*Conditions Present During Pregnancy for Live Births Induced by Oxytocin, by Type of Service, New York City, 1955*

Condition Present During Pregnancy	Induced Deliveries, No.			Induced Deliveries, %		
	Total	Private Service	Ward Service	Total	Private Service	Ward Service
Preeclampsia	495	320	175	43.1	38.6	54.5
Eclampsia	16	6	10	1.4	0.7	3.1
Hypertensive disease	97	75	22	8.5	9.1	6.9
Uterine bleeding not associated with labor	137	114	23	11.9	13.8	7.2
Pyelitis	23	17	6	2.0	2.1	1.9
Nephritis	12	9	3	1.0	1.1	0.9
Heart disease	43	37	6	3.7	4.5	1.9
Diabetes	40	19	21	3.5	2.3	6.5
Syphilis	8	6	2	0.7	0.7	0.6
Tuberculosis	11	5	6	1.0	0.6	1.9
Rubella or other viral infection	14	12	2	1.2	1.4	0.6
Injury or operation	22	21	1	1.9	2.5	0.3
Neoplasms	30	27	3	2.6	3.3	0.9
Other conditions	201	160	41	17.5	19.3	12.8
Total	1,149	828	321	100.0	100.0	100.0

Among the 441 unsuccessful inductions, 222 (50%), of deliveries were by cesarean section. In this group 54 patients were given a trial of labor with use of oxytocin for a period of three hours or more. Twenty-six of these were in labor more than 12 hours before termination by cesarean section. It appears that a significant number exceeded a trial period of less than three hours. Of these 54 patients subjected to long trial periods of labor, 11 had received oxytocin electively.

Where "successful" was stated, 72 were delivered by cesarean section. This may indicate either an error in filling out the certificate or a misinterpretation of the term successful on the part of the doctor filling out the certificate (tables 8 and 9).

Premature Births Induced by Oxytocin.—For 1955-1956, more than 6% of all live births induced with oxytocin were premature as compared with 8.7% for all live births in New York City. On the ward services, the premature rate was 11.5%; however for those induced, the rate was higher (15.6%).

Of the 29,381 total premature live births in New York City for 1955-1956, 1,025 (3.5%) followed induction by oxytocin. Of these, 281 (27.4%) were the result of elective induction. Premature births associated with elective induction were highest in the months of June, July, August, and December. It is highly probable that labor was induced prematurely in these patients who might otherwise have gone to term (table 10).

Perinatal Mortality.—The perinatal mortality for 1955 in the induced private patients was 2.8%. For the remainder on the private services it was 2.2%. On the ward service the perinatal mortality was much higher for the induced group than for the rest (16.4% as compared with 3.8%). The much higher perinatal mortality on the ward services for the induced group may be due to the fact that oxytocin was used largely in cases in which there were complications such as toxemia, partial separation of the placenta, and other therapeutic indications.

TABLE 7.—*Live Births by Mode of Delivery and Service, New York City, 1955 and 1956*

	Induced Deliveries				Other Deliveries			
	Private Service		Ward Service		Private Service		Ward Service	
Mode of Delivery	No.	%	No.	%	No.	%	No.	%
1955								
Spontaneous delivery	2,928	42.5	427	53.1	50,892	52.5	39,429	67.8
Forceps	3,579	51.9	286	35.6	35,908	37.1	13,721	23.6
Breech	130	1.9	31	3.9	3,055	3.2	1,906	3.3
Cesarean section	155	2.2	35	4.4	5,985	6.2	2,183	3.8
Other	12	0.2	1	0.1	179	0.2	132	0.2
Not stated	86	1.3	24	2.9	876	0.8	822	1.3
Total	6,890	100.0	804	100.0	96,895	100.0	58,193	100.0
1956								
Spontaneous delivery	3,170	44.1	569	53.6	49,963	52.4	39,519	66.3
Forceps	3,650	50.8	383	36.1	35,472	37.2	14,299	24.0
Breech	153	2.1	32	3.0	3,066	3.2	1,969	3.3
Cesarean section	135	1.9	47	4.4	5,870	6.1	2,293	3.9
Other	9	0.1	4	0.4	182	0.2	147	0.2
Not stated	71	1.0	26	2.5	830	0.9	1,373	2.3
Total	7,188	100.0	1,061	100.0	95,383	100.0	59,600	100.0

The perinatal mortality for the spontaneous and forceps deliveries after induction (0.5 and 0.2%) is lower than for those not induced (2.8 and 1.3%). In these cases the use of oxytocin was limited to a highly favorable group where a low perinatal mortality generally prevails and where oxytocin was used largely for elective rather than for therapeutic reasons. (Perinatal mortality as herein calculated =[fetal deaths after 28 weeks gestation+infant deaths under 7 days]÷[fetal deaths after 28 weeks gestation+total live births]×1,000. Perinatal mortality data for 1958 are not available at the time of this report.)

The perinatal mortality for the induced deliveries on the private and ward services combined is higher than for the deliveries without induction. This difference is due entirely to the significantly higher perinatal mortality associated with breech deliveries and cesarean sections. For these two categories of breech and cesarean section it was observed that oxytocin was used predominantly for therapeutic indications. In a group of 206 breech deliveries where induction was used, there were 57 perinatal deaths with a perinatal rate of 27.7%. This rate is much higher than that found for breech deliveries where oxytocin was not used (16.6%). In a group of 201 cesarean sections where induction was attempted, there were 20 perinatal deaths with a perinatal rate of 10.0% as compared with a perinatal rate of 5.2% for cesarean sections where oxytocin was not used.

Puerperal Mortality.—In 1955-1956 there were 203 puerperal deaths reported; 103 fetuses were of 28 weeks' gestation or over. It is important to note that puerperal deaths have been encountered in reviewing hospital records where use of induction was not recorded on the birth or fetal death certificates, although oxytocin had been administered. Furthermore, an analysis limited to a study of deaths due to puerperal causes has its shortcomings in excluding patients who survived although they had developed serious complications after the administration of oxytocin. Several case reports are cited in which the administration of oxytocin for the induction of labor was believed to contribute to mortality.

CASE 1 (hypofibrinogenemia, amniotic fluid embolism). —A 23-year-old woman, gravida 3, para 2, blood type A, Rh+, was a private patient with an uneventful prenatal course. She was electively induced at term (40 weeks) with intravenously given oxytocin, 10 units per 1,000 cc. of 5% glucose solution. She had a rapid labor, proceeding from 1 cm. cervical dilatation to sudden precipitous delivery of a stillborn fetus, including the simultaneous delivery of the placenta, in the course of one hour and five minutes. The fetal heartbeat was stated to be normal until 10 minutes before delivery, after which time it was no longer heard. The delivery was followed by severe uterine hemorrhage with failure of the blood to clot. Visual examination of the cervix at this time revealed no evidence of laceration. The patient received 8 units of blood (4,000 cc.) and 10 Gm. of fibrinogen before good clotting resulted. This patient's blood pressure could be maintained at adequate levels only by the use of dilute intravenously given levarterenol (Levophed) bitartrate solution. A lower nephron nephrosis developed. This condition became progressively more severe, resulting in death six days after delivery. Postmortem examination revealed lower nephron nephrosis, pituitary necrosis, and pulmonary amniotic fluid embolism.

TABLE 8.—*Results in Induced Deliveries, by Mode of Delivery, New York City, 1955 and 1956*

	Induced Deliveries, 1955				Induced Deliveries, 1956			
Mode of Delivery	Total	Successful	Not Successful	Not Stated	Total	Successful	Not Successful	Not Stated
No operative procedure	3,355	2,731	50	574	3,739	3,066	49	624
Forceps deliveries	3,865	3,233	49	583	4,033	3,308	50	675
Breech deliveries	161	125	6	30	185	146	5	34
Version	10	10	...	...	13	8	...	5
Cesarean section	190	38	116	36	182	34	106	42
Other operative procedures	3	1	...	2	...	...	...	...
Mode not stated	110	84	6	20	97	69	4	24
Total	7,694	6,222	227	1,245	8,249	6,631	214	1,404
Percentage	100.0	80.9	3.0	16.1	100.0	80.4	2.6	17.0

Comment.—While it has been observed that, on occasion, when oxytocin has not been used, tumultuous rapid labor will result in a condition similar to that described above, it is definitely felt that the sequence of events in this fatal case were initiated by the use of oxytocin. Similar cases have been encountered in the course of review of hospital records in obstetric services over the past several years where hypofibrinogenemia resulted after the use of intravenously given oxytocin for induction and/or stimulation of labor, particularly in toxemias of pregnancy. Many of these patients have survived with the administration of adequate fibrinogen and blood replacement. These cases have not been reported in the literature.

Case 2 (ruptured uterus).—A 27-year-old woman, gravida 7, para 4, had an uneventful prenatal course with normal laboratory findings. She was admitted to the hospital at 34 weeks' gestation with ruptured membranes and mild uterine contractions. It was stated on the record that "because of desultory ineffectual contractions" oxytocin, 10 units per 1,000 cc. of 5% glucose solution, was administered by drip induction. The presentation in this case was left occipitotransverse. The cervix was soft, 50% effaced, and 2 cm. dilated. After three hours and 15 minutes of labor the patient spontaneously delivered a 2,268-Gm. (5-lb.) living infant and immediately went into severe shock. The patient received 10 units of blood, administered under pressure, and a hysterectomy was promptly performed. Examination revealed uterine rupture with massive retroperitoneal hemorrhage. The patient died on the operating room table.

Comment.—This patient had a premature infant with a gynecoid pelvis which was adequate. It is highly unlikely that this accident would have occurred spontaneously. Although the experienced obstetrician is aware that uterine rupture may occur spontaneously, particularly with increased parity, the risk of this complication is compounded by the use of a potent agent such as oxytocin.

Table 9.—*Induced Deliveries Unsuccessfully Performed by Cesarean Section, by Indications for Induction of Labor and Duration of First Stage of Labor, New York City, 1955 and 1956*

Indications for Induction	1955 Deliveries, Total	1955 Duration of Labor, Hr. <3	3 to 12	12 to 24	>24	No Labor	Not Stated	1956 Deliveries, Total	1956 Duration of Labor, Hr.* <3	3 to 12	12 to 24	No Labor	Not Stated
Not induced	1	...	...	1	...	...	...	...	...	...	...	...	...
Elective	21	...	4	2	2	13	...	14	...	...	3	10	1
Therapeutic	38	3	6	4	3	20	2	37	2	5	3	25	2
Other	9	...	1	...	...	8	...	6	...	...	1	5	...
Uterine bleeding	1	...	...	...	...	1	...	5	...	1	...	4	...
Toxemia	28	...	3	...	...	23	2	30	...	3	2	25	...
Indications not stated	18	...	3	3	1	11	...	14	...	2	1	10	1
Total	116	3	17	10	6	78	4	100	2	11	10	79	4

* In no case did labor continue for more than 24 hours.

Case 3 (breach presentation, ruptured uterus).—A 21-year-old primipara with a breech presentation, left sacroanterior, was admitted to the hospital at term for elective induction of labor. The record noted an adequate gynecoid pelvis. After three and one-half hours of "good labor" after administration of oxytocin, the patient went into shock. On examination, the fetus was recognized to be in the upper abdomen and an immediate laparotomy was performed. Approximately 3,000 cc. of blood was found in the peritoneal cavity. A living 3,200-Gm. (7-lb.) male fetus was extracted from the peritoneal cavity. It was observed that the uterus was ruptured through the fundus. The patient received 14 units of blood, and the maintenance of her blood pressure was assisted by an intravenous solution of levarterenol. The patient then appeared in fair condition with a blood pressure of 110/86 mm. Hg and pulse rate 120 per minute. However, the urine output was diminished, and 12 hours postoperatively the patient's skin was cold and clammy. The hematocrit reading was 38%, blood pressure 100/70 mm. Hg, and blood platelet count 112,000 per cubic centimeter. Although the blood clotted and the prothrombin time was normal, the patient died 27 hours after operation due to massive retroperitoneal hemorrhage which was demonstrated at postmortem examination.

Comment.—This case illustrates the outcome of injudicious elective induction of labor with oxytocin in a primipara with a recognized breech presentation, resulting in a ruptured uterus.

Additional cases of ruptured uterus have been encountered in association with the use of intravenously given oxytocin for induction. Space does not permit the detailed accounts of at least 12 known cases of serious complications of ruptured uterus, severe hemorrhage with or without hypofibrinogenemia, and amniotic fluid embolism after the elective induction of labor with oxytocin. Most of these patients fortunately survived after prompt detection of the complication and immediate therapy. It is important to note that the above abstracted cases occurred on well-equipped obstetric services with qualified obstetricians.

Although all experienced, well-trained obstetricians are aware of the potential danger in the use of oxytocin, errors in judgment in the use of this drug and its occasional unpredictability will continue to add to the catastrophies presented.

Comment

For the years 1955 and 1956 oxytocin was used for the induction of labor in 4.9% of all deliveries in New York City, as reported on the birth certificates, and in 6.6%, as reported in the hospital questionnaire form. These figures are much higher than those reported by Hellman and co-workers [5a] in their analysis of 63,276 deliveries in 10 hospitals from 1951 through 1955 wherein it was stated that intravenously given oxytocin was used in 1.8% of the cases for the induction of labor. Elective induction accounted for 52% of all the oxytocin-induced deliveries on private services in New York City.

An outstanding finding which emerged from analysis of the data is the occurrence of peaks in the use of oxytocin in private patients for the induction of labor in the months of July, August, and December. This highlights the fact that it is extensively used for the convenience of the obstetrician and/or the patient. Various reports [6] from the literature indicate that convenience is a factor in the elective use of oxytocin for the induction of labor. Hellman states, "It seems highly improbable that these well trained and seasoned obstetricians would use a potentially dangerous drug to satisfy personal convenience." Willson,[7] in a study of 180 cases of elective induction with intravenously given oxytocin, concludes that its use is seldom justified in normal pregnancy.

The following factors are related to the use of oxytocin.

Ruptured Uterus.—It would appear that, in the puerperal deaths herein described, the use of oxytocin led to rupture of the uterus. Case reports corroborate the sequence of ruptured uterus occurring after elective use of oxytocin.[8]

Uterine Hemorrhage.—Within the limitations of the data obtained from certificates, the problem of postpartum or intrapartum hemorrhage is not ascertainable except as associated with a puerperal death. Sotto and Wildhack[9] indicate a higher proportion of severe hemorrhages after the elective use of oxytocin. The question of hypofibrinogenemia has been raised and is suggested in our review of puerperal deaths.

Table 10.—*Premature Live Births, Induced by Oxytocin, by Month of Delivery, New York City, 1955 and 1956*

Month of Delivery	Induced Deliveries, 1955				Induced Deliveries, 1956			
	Total		Elective		Total		Elective	
	No.	%	No.	%	No.	%	No.	%
January	27	5.7	4	0.8	53	9.8	11	2.0
February	27	5.2	1	0.2	42	7.1	12	2.0
March	39	7.0	11	2.0	44	6.2	11	1.5
April	48	7.5	10	1.6	40	6.6	6	1.0
May	40	6.3	17	2.7	41	6.2	8	1.2
June	43	6.5	13	2.0	47	6.6	16	2.2
July	47	6.5	17	2.3	42	5.3	16	2.0
August	51	6.4	24	3.0	40	5.3	12	1.6
September	48	7.9	12	2.0	42	6.3	7	1.1
October	28	4.4	4	0.6	40	5.7	9	1.3
November	45	6.7	17	2.5	33	5.1	9	1.4
December	64	8.2	18	2.3	54	6.4	16	1.9
Total	507	6.6	148	1.9	518	6.3	133	1.6

Perinatal Mortality.—Much more information needs to be added to our findings, which suggest that in cesarean section and breech deliveries the prior use of oxytocin appears to increase mortality. Several reasons may be postulated for this:

1. Where oxytocin was given intravenously, an indicated cesarean section was possibly delayed, resulting in fetal distress. 2. In patients with borderline pelvic measurements, a trial of labor may be unduly prolonged when oxytocin is used and result in fetal damage. This is in agreement with the views expressed by Cosgrove and Weaver.[10] 3. The use of oxytocin may result in fetal distress by causing prolonged uterine contraction or tumultuous labor.

On the other hand, although mortality in the case of spontaneous delivery after use of oxytocin is not increased, a matched control group is needed to compare induced spontaneous deliveries with those not induced, where the same socioeconomic factors and level of obstetric care prevail.

Fetal Distress.—Trauma to the infant, short of being fatal, is not ascertainable from certificate data. Seven cases of fetal distress after the elective use of oxytocin which necessitated cesarean section have been mentioned above. This would substantiate the belief that occasionally the fetus is subjected to needless damage. Long-term follow-up of such individuals would be of invaluable help.

Many of the questions raised here regarding the use of intravenously given oxytocin and its effect on the mother and upon the infant remain unanswered. It is hoped that this study will stimulate further investigations on the use of oxytocin for acceleration and/or induction of labor.

Summary

An analysis has been made of the use of intravenously given oxytocin (Pitocin) in New York City for 1955-1956, as ascertained by birth and fetal death certificates and by questionnaire. Oxytocin was used for induction in 4.8% of all live births, as determined from certificate data. Induction of labor with intravenously given oxytocin occurred primarily on the private services of the voluntary hospitals. Of all elective inductions, 95.1% occurred on private services. Labor was induced by use of oxytocin almost five times more frequently in the private patients than in the ward patients.

A geographical variation was noted in the frequency of use of oxytocin for the induction of labor. Of the five boroughs in New York City, Brooklyn was recorded as having the highest incidence. A marked seasonal variation in the use of oxytocin was observed on the private services. The peak months were July, August, and December. Elective induction was chiefly responsible for the seasonal variation observed. No such variation occurred on the ward services.

Of the 1,025 premature infants born after the use of oxytocin, 281 (27.4%) were born after elective induction. The highest incidence of premature births after elective induction occurred in June, July, August, and December. The infant mortality rate was almost twice as high for infants delivered by cesarean section where oxytocin had been previously used as compared with those delivered by cesarean section where previous induction had not been attempted. In several cases of puerperal mortality oxytocin appeared to have initiated an unfortunate sequence leading to rupture of the uterus, hypofibrinogenemia, and uterine hemorrhage.

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PREVENTION OF INFECTION OF URINARY TRACT IN PRESENCE OF INDWELLING CATHETERS

DESCRIPTION OF ELECTROMECHANICAL VALVE TO PROVIDE INTERMITTENT DRAINAGE OF THE BLADDER

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and

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Catheters kept in the urinary bladder as long as four days provoke bacteriuria in almost every case. The technique here described prevents this complication by continuous irrigation with 0.25% acetic acid through a catheter with three lumens. One passage permits distention of the retaining balloon; the other two passages are for inflow and outflow. The method was successful in more than 100 patients. The rate of inflow of the acetic acid solution was roughly equal to that of urine production, but it was adjusted so that the effluent was kept at pH 5.0 or less and the bacterial count at less than 1 million per milliliter. Outflow was interrupted periodically by use of an electromechanical valve to permit filling of the bladder and avoid prolonged contraction. In some patients it was possible to leave the catheter in situ as long as 60 days without inducing bacteriuria.

When an indwelling catheter has been in the bladder for 24 hours, the incidence of bacteriuria in patients whose urines were previously sterile is about 50%. After four days of constant catheterization 98-100% of patients develop 100,000 or more bacteria per milliliter of urine.[1] The hazards of catheterization have been widely recognized and the medical profession has been cautioned against the indiscriminate use of indwelling catheters.[2] On the other hand, the indwelling catheter is often indispensable to the management of many clinical conditions. The desirability of using the indwelling catheter without inducing bacteriuria is manifest.

The bacteriuria that follows the use of indwelling catheters is due to the constant entry of bacteria into the bladder when the catheter is in place. The probable route of entry of the bacteria is the film of exudate that forms in the urethra in response to the presence of the catheter.[3] This film is an excellent culture medium for bacteria and links the fecal

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reasonable ppose that proper choice of the
diameter of a catheter and careful technique in insertion may delay the entry of bacteria. Cleansing the bladder of bacteria promptly after they have entered it can be achieved if the bladder is rinsed with an antibacterial solution so that bacterial multiplication cannot occur. If antibacterial solutions are to be useful for such a purpose, they should be nontoxic, relatively inexpensive, active against all of the bacterial species that may be found in the bladder, and unlikely to permit resistant strains to emerge.

Acetic Acid as Bacteriostatic Agent

Acetic acid satisfies these conditions. It is a potent bacteriostatic agent. At pH 5.0, which is not lethal for most pathogens of the urinary tract, as little as 0.01 M (0.06%) acetic acid will sterilize a broth culture of Escherichia coli. None of the urinary tract pathogens so far tested has resisted 0.02 M acetic acid at pH 5.0. The antibacterial action of organic acids has been known for many years, and acetic acid has been a standard rinsing solution in douches and bladder rinses. Its limitations have been few, but they are critical. Chief among these is that the antibacterial action of acetic acid is apparently linked to the number of unionized molecules in solution; if the pH is permitted to rise, the antibacterial action falls off sharply. Furthermore, the antibacterial action of acetic acid requires prolonged contact between the acid and the bacteria, so that more or less continuous presence of acetic acid in the bladder must be maintained.

The simplest means for providing continuous administration of acetic acid is by the use of an ordinary double-lumen indwelling catheter. This type of catheter actually has three lumens: one for distending the retaining balloon and two running from the interior of the bladder. A solution of 0.25% acetic acid (prepared by adding 2.5 ml. of glacial acetic acid to 1 liter of sterile water) drips into one of these tubes, and the mixture of acid and urine leaves through the other. The rate of flow of the acid is adjusted so that the effluent is kept at pH 5.0 or less and the bacterial count at less than 100,000 bacteria per milliliter of urine. The pH can be tested by inserting a strip of pH paper, such as nitrazine paper, into the effluent. The bacterial count is determined by microscopic examination of a stained drop of uncentrifuged effluent. If no bacteria are seen, the bacterial count is generally less than 100,000 per milliliter.[1] The bacterial count can be determined more precisely by standard pour plate colony counts of serial dilutions of the effluent. Only rarely, if adequate amounts of acetic acid are used, will any bacteria be found in the culture.

The procedure outlined above is highly effective if the flow of acetic acid is sufficiently rapid. Ordinarily a flow of 0.25% acetic acid equal to the rate of urine flow is adequate. When a highly alkaline urine is encountered, as in Proteus infections, the rate of flow may be increased. If necessary, a higher concentration of acetic acid, such as 0.5%, may be used. In extremely difficult situations, in which the urine has remained alkaline despite rinsing of the bladder with acetic acid, a stronger acid, such as 0.25% lactic acid, may be used to acidify the urine to pH 5.0 or less. Acetic acid may then be substituted for lactic acid, since on a molar basis acetic acid is about 10 times as active as lactic acid as a bacteriostatic agent at pH 5.0.

Drainage System for Bladder

The continuous drainage system just described will maintain the bladder free of bacteria if properly managed. However, after two or three days, the bladder may become so contracted that when the catheter is removed the patient will often complain of frequency and marked pelvic discomfort, because of the small volume of the bladder. The effects of contraction of the bladder may be circumvented by providing intermittent filling of the bladder to a physiological volume. This may be done effectively by the use of tidal drainage, which supplies both a physiological stimulus and a constant supply of antibacterial fluid to the bladder. Unfortunately, tidal drainage requires an apparatus that is sufficiently complex to have aroused substantial resistance from house staff and nursing staff alike. Some simplification of this approach is desirable. In addition, tidal drainage often will not work in individuals with hypotonic or irritable bladders.

The two-way catheter drainage system that has been described may be modified to permit the bladder to increase its volume. Initially, the effluent tube was clamped and released for only five minutes every hour, permitting accumulation and periodic discharge of the contents of the bladder. In this manner, the bladder could be distended to hold a volume of several hundred milliliters, depending upon the rates of flow of urine and of acetic acid into the bladder. However, the personnel problems involved in the manual control of the clamp were such that it seemed desirable to have this task performed electromechanically.

Electromechanical Device

An electromechanical device for controlling the discharge of fluid from the bladder is shown in the figure. It consists of a motor-driven timer, which actuates a solenoid-operated clamp. The effluent tube is placed within the clamp, which is in the open position when no electrical current is flowing. When the switch is turned on, the clamp shuts and no release of fluid from the bladder can occur. The timer opens the clamp at periodic intervals. The present apparatus, which is the result of testing of several alternatives, provides four timing cycles. The clamp may be kept closed for 55 minutes and opened for 5 minutes, or it may be closed for 25 minutes and opened for 5 or closed for 15 minutes and opened for 15. The device can be hooked to the bedrail or bedspring, is virtually noiseless, and is "fail safe" (any mechanical or electrical failure causes the clamp to open automatically).

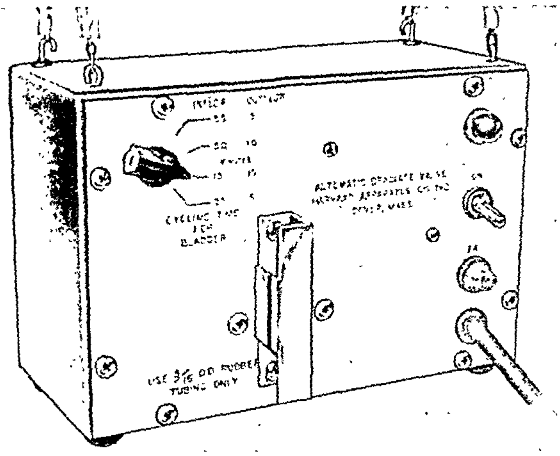
The apparatus has been used in more than 100 patients who have required indwelling catheters. Less than 10% of patients whose catheters have been managed by this method have developed bacteriuria, whereas 100% of patients given saline instead of acetic acid have developed bacteriuria.[4] Patients with indwelling catheters have been maintained for as long as 60 days by this procedure without any bacteria being found in the bladder.

In practice, one lumen of the indwelling catheter is attached to a bottle fitted with a dropping device and containing 0.25% acetic acid. The rate of flow into the bladder is controlled by an ordinary tubing clamp. The effluent from the bladder is collected in a receptacle beneath the bed. The rubber tubing passing from the catheter to the collecting bottle is placed in the clamp of the electromechanical valve. For most purposes the cycle is kept at 55 minutes closed and 5 minutes open. If the capacity of the bladder is small, a shorter cycle may be used. The 15-minute cycle has been particularly useful in the management of pyelostomies and in dealing with indwelling catheters in small children.

No important difficulties have arisen thus far in the use of this device. The clinical results, which will be the subject of a more detailed report elsewhere, have indicated that the acid rinse as presently used induces microscopic hematuria in about 5% of patients. About 1% develop pelvic distress and gross hematuria. Further improvements in the nature of the antibacterial rinsing fluid are expected to diminish the incidence of these local reactions.

Summary

In order to avoid infection of the urinary tract during indwelling catheterization, the bladder should be rinsed constantly with an antibacterial solution. Dilute acetic acid (0.25%) is an adequate solution if its flow is sufficiently rapid to provide a pH of less than 5.0 and bacterial counts in the urine of less than 100,000 bacteria per milliliter. The acetic acid rinse is conveniently administered through one lumen of a two-way catheter and the acidified urine is discharged through the other. An electromechanical valve may be used for providing intermittent drainage of the bladder simply and reliably.



Electromechanical device for controlling discharge of fluid from bladder.

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AMNESIA-ANALGESIA FOR THE MANAGEMENT OF CHILDREN TOO YOUNG TO COOPERATE

FURTHER OBSERVATIONS

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Some months ago I[1] reported the results of application of a procedure which my colleagues at the Mayo Clinic in 1957 asked me to develop for the management of cardiac catheterization in children too young to cooperate. In that report I based my observations on experience with 36 children, 9 months to 12 years old, who had cardiac defects and defects of the great vessels. Fifty-one other children were managed by the same procedure, plus the use of anesthesia with nitrous oxide, oxygen, and ether, preparatory to tonsillectomy and adenoidectomy or operations on the eye. My series now includes 133 children who underwent cardiac catheterization and 100 who underwent other operations which demand a degree of tranquility and cooperation from the patient.

It is emphasized again that the procedure in question does not consist primarily of anesthesia alone. Rather, it is a special application of both analgesia and amnesia. The important aspect is the fact that the agents used do not interfere with the test or examination being carried out, as they would if they were primarily anesthetic agents administered, particularly by inhalation. The patient breathes either air or oxygen throughout the test or examination, so that it is possible for the physician during cardiac catheterization, for instance, to interpret physical data readily, to carry out Van Slyke tests, and to reach an unimpeded decision as to the lesion or lesions present, provided that technical difficulties arising during the course of the test do not complicate matters unduly.

Cardiac catheterization, like many other diagnostic and therapeutic procedures, poses especially difficult problems for the anesthesiologist when the patient is too young to cooperate. The procedure here outlined consists of a sequence of steps whereby the requisite degree of tranquility, analgesia, and amnesia can be attained without interfering with the tests or examinations being carried out. Upon this background it is possible to superpose anesthesia with nitrous oxide, cyclopropane, or ether for short periods when necessary. Exact calculation of dosages is essential. Applied in 133 cases of cardiac catheterization and 100 comparable operations of other kinds, this plan has reduced to a minimum the respiratory and other reflex disturbances which otherwise make it difficult to interpret results.

Method

The mechanics of the procedure are set forth in the table. First of all, the pediatrician furnishes an estimate of the degree of risk of cardiac catheterization, based on a scale of 1 to 4 in which 4 is the gravest risk. Next, the parents or relatives of the child are told specifically what is to be done and what the risk is. Then I weigh the child myself. This is of prime importance, since experience has shown that in some instances only estimates of body weight will be furnished by the referring physicians. Catheterization of the heart then proceeds, after which I receive the child into my care, where he remains until I send him to the hospital or until the parents or relatives take him home.

The three factors are the weight of the child, the passage of time checked carefully by the clock, and abatement of the movements of the child. The chief hazard in this method involves exact measurement of the dose of the drug from the container in which the manufacturer supplies it. The smaller the child, the more difficult it is to measure exactly the required dose. Only recently have I been able to obtain a mixture of levorphanol (Levo-Dromoran) tartrate and levallorphan (Lorfan) tartrate compounded in such a manner as to assure me that 0.2 cc. per 10 lb. of body weight of the child is the correct dose. I also have been able to obtain promethazine (Phenergan) hydrochloride in a correspondingly correct dilution and alphaprodine (Nisentil) hydrochloride and proheptazine (Wy 757) as well. Each time the formula has been modified, the results have been unsatisfactory from the standpoint of both the management here described and the test itself.

To calculate the dose of thiopental (Pentothal) sodium to be administered rectally, the actual weight of the child in pounds is used. To calculate the dose of drugs to be administered by injection, the weight in pounds generally is lowered to the next even number in units of 10 or to make the figure in units of 10 or halfway between. That is,

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if a child weighs 41 lb., the weight employed in the calculation would be 40 lb. If the weight were 46 lb. the figure 45 would be used for calculation of the dose, or if the weight were 49 lb. the figure 50 might be used. Any arbitrary increase in the weight for purposes of calculation of the dose can be used only when the patient is relatively robust.

Some children do not, because of intrinsic physiological factors or deficiencies of which we are not yet aware, tolerate the procedure well, and difficulties will arise when such patients are managed by the method described. Some vomit once or twice after they awaken, and this applies to those who have not undergone cardiac catheterization as well as to those who have, indicating that the vomiting may not be referable to the heart. Some of the premonitory signs are known. A child who holds his breath probably will not adapt himself satisfactorily to the procedure, for such an action has been seen to exert an adverse effect on the circulation. Heavy crying on the part of a child also is a sign of impending difficulties with the circulation. A child who is in a very unsatisfactory state of debilitation obviously is not an ideal candidate for the method.

The blood pressure of three children who manifested these signs decreased precipitately to 22, 28, and 98 mm. Hg; one died 12 hours after cardiac catheterization, one died 15 hours after the procedure, and one died immediately after the procedure. Studies are under way to elicit additional causative factors in such difficulties.

Following is an illustration of a difficulty that can arise. One of the assistants, without consultation, decided to administer a small quantity of thiopental sodium intravenously through the cardiac catheter. The result was a sudden depression, with a decrease in blood pressure which is entirely

OUTLINE—MAY BE HAZARDOUS IF NOT FOLLOWED EXACTLY

NOTE: BEFORE CATHETERIZATION, THE ANESTHESIOLOGIST HIMSELF SHOULD WEIGH THE PATIENT AND EXPLAIN TO THE RELATIVES WHAT IS TO BE DONE. IN THE COURSE OF CATHETERIZATION, HE SHOULD GO OUT AND REASSURE THE RELATIVES NOW AND THEN.

Procedure:

	Step	Agent*	Dose		Route	Remarks
			Mg.	Relation to Body Wt.		
Preoperative	1	thiopental (Pentothal) sodium	15	per 1 lb.	rectal	
	2	Wait 5 to 10 min. for thiopental sodium to take such effect that patient will not remember IM injections of step 3				
	3	Step 3 consists of injection, at one time, of 4 drugs, all mixed together in one syringe, as follows (a, b, c, d):				
	a	levorphan (Levo-Dromoran) tartrate	0.2 WARNING see remarks	per 10 lb.	IM	Even if a child weighs more than 100 lb., if he is 10 yr. of age or less, dose of levorphan MUST NOT EXCEED 1 mg. Give NO additional levorphan for same procedure
	b	levallorphan (Lorfan) tartrate	0.1	per 10 lb.		Mixture given in step 3 is not clear. Do not be alarmed by milky appearance. It can be used without being cleared. However, it can be cleared by mixing with 1 cc. of 1% procaine hydrochloride
	c	promethazine (Phenergan) hydrochloride	2.0	per 10 lb.		
	d	proheptazine (Wy 757) or alphaprodine (Nisentil) hydrochloride	1.0	per 10 lb.		
	4	Wait 20 min. for analgesia, prospect of amnesia, or both to develop				
Operative	5	Infiltrate with local anesthetic line of incision for venostomy				
	6	proheptazine or alphaprodine	1.0	per 10 lb.	IM	This step is necessary IF CHILD IS RESTLESS, as most children are
	7	*Wait 5 min. in expectation that child will become sufficiently quiet to permit initiation of cardiac catheterization and will remain quiet for 1 to 2 hr.* If child is not sufficiently quiet for cardiac catheterization to start, or if catheterization is in progress and child becomes unduly restless, give following:				
	a	proheptazine or alphaprodine	1.0	per 10 lb.	IM	Dose may be given again at intervals of 45 min. to allay restlessness
	b	If patient moves within 1¾ to 2 hr. after the first enema of thiopental (see step 1), and if the procedure is expected to take 3 to 5 hr. (NOT if procedure is expected to be short: i. e., 2-3 hr.) repeat step 1 and, if necessary to keep patient quiet, step 7a.				
Postoperative	8	After catheter tip has been removed from heart, but before it has been removed from vein, give following drugs:				
		bemegride (Megimide; 3-ethyl-3-methylglutarimide) and amiphenazole (Daptazole)	10 ABSOLUTE 30†	WITHOUT RELATION TO BODY WEIGHT	via catheter	*Five min. after this dose is given, if necessary to arouse patient, same dose, BUT GIVEN INTRAMUSCULARLY, may be used once again*
	9	Now, because of congenital cardiac defect and stress of procedure, begins a period that may be HAZARDOUS. Usually, about 1 min. after bemegride is given, patient will arouse sufficiently to answer questions. Thereafter, for 1 to 2 hr., he should be in state much resembling normal light sleep, from which he can be easily aroused. BUT if BLOOD PRESSURE FALLS and CYANOSIS develops, give following:				
	a	oxygen			inhalation	*Five min. after this dose, if necessary to raise blood pressure more and to produce signs of arousal, same dose by same route may be given once again.* Then, if respiration is not good, give 0.1 mg. of levallorphan intravenously
	b	*mephentermine (Wyamine) sulfate* or methylphenidate (Ritalin) hydrochloride	7.5 ABSOLUTE 7.5 ABSOLUTE	WITHOUT RELATION TO BODY WEIGHT	IM	

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* Until the manufacturers concerned offer the following agents in the precise quantities required for the procedure in question, I use the following proportions:

levorphan	1.0 mg.
levallorphan	0.5 mg.
alphaprodine	5.0 mg.

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

proheptazine or alphaprodine	5.0 mg. (steps 6 and 7a)

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

promethazine	10.0 mg.

solvent to make 1 cc.; administered in a dose of 0.2 cc. per 10 lb. body weight

† If child weighs less than 50 lb., dose of amiphenazole may be reduced to 15 mg.

OUTLINE—MAY BE HAZARDOUS IF NOT FOLLOWED EXACTLY

unsatisfactory as far as the test is concerned. Moreover, such an action is quite unsatisfactory to me, since I have no way to control the dose administered. Therefore, further intravenous injections have been disallowed. If the child is too active, thiopental sodium is administered again by rectum.

One of the questions that has been answered more or less since the preliminary report[2] has to do with the fact that about 10% of these children are resistant to the action of the thiopental sodium enema and the hypodermic injection. It now appears certain that, if the child is still crying and moving 15 minutes after the first rectal administration of thiopental sodium and also 10 minutes after the hypodermic injection, a second full dose of thiopental sodium should be administered rectally. In only one instance in this series was the child sufficiently unconscious that five minutes after the rectal administration of thiopental sodium the child appeared to have an overdosage. In this case nothing further was used in a procedure that lasted two and one-half hours. This emphasizes the importance of the body movements of the child.

A possible criticism of this method might be that it causes the patient to sleep for two or three hours after the test has been completed. However, such an effect is not hazardous, and, if it constitutes a deficiency, the disadvantage is more than outweighed by the enhanced safety which the method provides.

I may point out that in this series I have had only two or three patients who were relatively overweight. Most of the patients have been underweight, and this may explain why the method has been so satisfactory. Nevertheless, even when the patient is overweight I am convinced that the statement, "Even if the child weighs more than 100 lb., if he is 10 years of age or less, the dose of levorphan must not exceed 1 mg.," is correct and should be observed scrupulously.

Applications Other Than in Cardiac Catheterization

This method also has been applied in almost 100 procedures other than cardiac catheterization. Irradiation therapy for retinoblastomas of the eye, heretofore a difficult anesthesia-analgesia-amnesia problem, is well suited to the technique I have described. There are three phases of this problem: (1) an initial period of surgical anesthesia of moderate length for implantation of seeds or needles, (2) an intermediate period of amnesia-analgesia extending several hours, during which the implant must not be disturbed, and (3) another period of surgical anesthesia of relatively short duration for the removal of the seeds or needles.

Thiopental sodium is administered rectally to the child on a basis of 15 mg. per pound of body weight. When a light sleep is evident, these agents are administered intramuscularly: 0.2 mg. of levorphanol, 0.1 mg. of levallorphan, 0.1 mg. of alphaprodine, and 2.0 mg. of promethazine, each per 10 lb. of body weight. This is an exacting technique: reference should be made to the accompanying table for the details. Venipuncture can be done with ease at this point, preferably with a plastic needle, so that fluids may be given continuously.

The patient is then anesthetized by gradually increasing the concentration of ether in an oxygen (3 liters) and nitrous-oxide (7 liters) mixture until a depth of anesthesia appropriate for intubation is obtained, at which time an endotracheal tube is passed orally. Surgical anesthesia is maintained while the radon seeds are implanted. After this, maintenance of inhalation anesthesia is discontinued and the endotracheal tube is removed. The child will then remain in a state of amnesia-analgesia for several hours without disturbance of the implanted radon or radium.

When radon or radium is to be removed, the patient again is anesthetized. Since this is a relatively short procedure, cyclopropane is the anesthetic agent of choice and endotracheal intubation usually does not appear justified. The recommended initial mixture is 6 liters of nitrous oxide, 3 liters of oxygen, and 1.5 liters of cyclopropane, administered by mask. When a surgical depth of anesthesia is reached, a tube is introduced into the nostril, away from the surgical field, and the other nostril and the oral airway are occluded. Inhalation anesthesia is maintained through the nasal tube, and the mixture of cyclopropane is adjusted to that minimal concentration which will be adequate for anesthesia. At cessation of the operation ventilation is begun by the administration of 100% oxygen. The child will arouse quickly but will lapse into a light sleep if left undisturbed for the immediate postoperative period.

For example, a 2-year-old child with retinal blastoma was put to sleep according to the method I have described and received nitrous oxide and oxygen while the eye was exposed and the radium seeds were implanted. In this case the rectal administration of thiopental sodium (100 mg. per cubic centimeter) was followed in exactly five minutes by injection of the four drugs concerned. Respiration was depressed for one and one-half minutes, no doubt as a result of the peak effect of the five drugs used. In this instance results probably would have been better had I waited a few more minutes before proceeding with the hypodermic injection. Three and one-half hours later the operation was concluded by exposure of the eye and removal of the radium. Under such conditions it probably would be wise to do venipuncture and to administer fluids intravenously throughout the procedure.

By means of this technique a difficult anesthetization problem is handled with ease. A minimum of depression referable to any one single agent will be noted, with a consequent minimal risk to the patient. This again emphasizes the value of the concept of balanced anesthesia.

Comment

I have been assured by pediatricians who refer such patients for the test and by physiologists who do the test that they are entirely satisfied with the results of this method of management, since it helps them to avoid technical errors which might otherwise make it difficult to interpret their data. The excellent respiratory action which the method provides is the result of the effect of levallorphan tartrate.

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Dr. Richard M. Hewitt aided in the preparation of the table.

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CLINICAL NOTES

SAFETY CLOSURE CAPS

SAFETY MEASURE FOR PREVENTION OF ACCIDENTAL DRUG POISONING IN CHILDREN

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The accidental ingestion of drugs causes 35% of deaths from poisoning in children 1 to 5 years of age. In this age group the incidence of poisoning from drugs is, however, far greater than that from household agents. Mellins and co-workers[1] reported the incidence of drug poisoning alone from the Chicago Poison Control Center as 50.6%. Recent figures from the National Clearing House, as reported by Cann and associates,[2] showed that 50% of the 4,000 cases reported from 29 poison control centers were due to the ingestion of drugs. Figures from the New York Poison Control Center are even higher—an amazing 70%.[3]

In 1956 over 3.5 billion dollars was spent for drugs in the United States, so there is little wonder that poisoning is so frequent in infants and children who learn by exploration, questioning, sampling, and trial and error. They are particularly susceptible to the accidental ingestion of brightly colored, attractively shaped and packaged, sugar-coated drugs of all kinds. This being the case, it should be apparent to everyone that all available safety measures and precautions should be utilized. It is imperative that physicians give more than lip service to this problem and that they stop suggesting that education is the only means of prevention. Precautionary labeling and safety closures are good measures, among others, in the prevention of these tragic accidents.

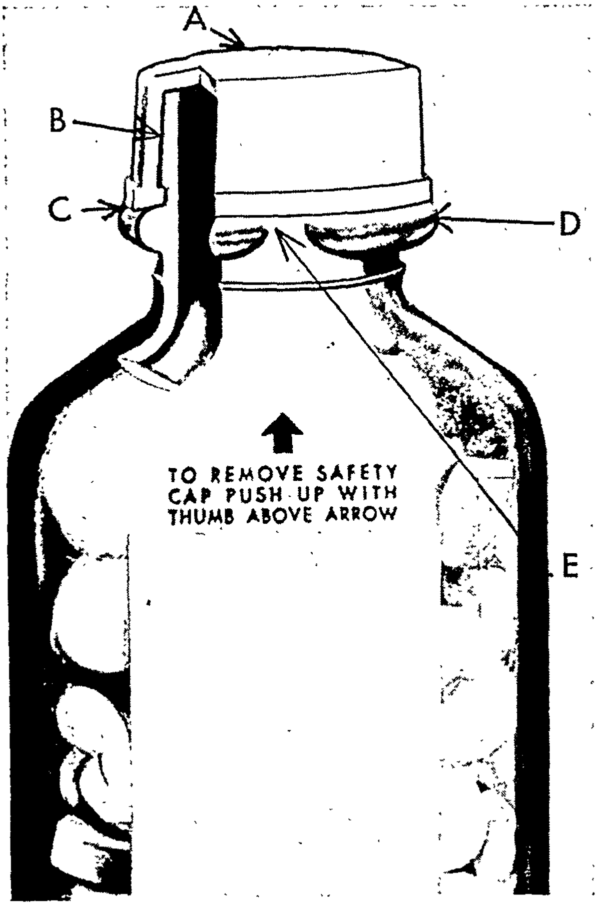
After trying out more than 14 different types of safety caps over a period of three years, two were finally selected for comparison with the conventional screw cap in 1,600 representative homes with children under 5 years of age. The objective of this survey was to determine which of the three closures would be most effective in reducing the chances of small children gaining access to aspirin in the containers kept in the home. At the same time, it also was necessary for these safety caps to be designed and constructed so that mothers could remove and replace them with a reasonable amount of ease and convenience.

Results of Survey

The following information was obtained at the completion of the survey: The A and B closures were equally difficult to remove by over 93% of the children in the survey, as compared to 66% in removing the screw cap. Only 33.8% of the children had difficulty in replacing the B closure, as compared to 56.8% for the A type and 38.9% for the screw cap. These figures imply that older inquisitive children, in replacing the B cap easily, can conceivably prevent younger infants in the family from gaining access to the contents of the respective bottle.

In the survey of mothers, difficulty in removing the closure was affirmed by over 67% for the A type, 16% for the B type, and 49% for the screw cap. When asked, "In regularly replacing the cap, do you feel that it goes on securely each time?" affirmative answers were given by 60% for the A type, 97% for the B type, and 81% for the screw cap.

As a safety measure, the difficulty that mothers encountered in replacing the A cap and the screw cap (i. e., resealing the bottle) is more significant than their difficulty in opening them, since a loose cap can mean an open container.



Safety closure of choice: *A*, wording on top, "Keep bottle out of children's reach," for adult caution; *B*, glass tapers to allow easy cap replacement; *C*, grip of cap under glass for tight seal and reseal; *D*, wide-design special glass bead, to help reduce biting off or pulling off by children; and *E*, bead opening (in front and back) for adult "thumb-off" removal.

The children's difficulty in removing the B cap and their mothers' ease in removing and replacing the B cap made it the closure of choice from the manufacturers' and the families' standpoint (see figure).

Although questionnaire responses are often disapproved of for definitive statistical data, and however impressive these figures are, one must always keep in mind that over 6% of the children under 5 years of age in the survey were able to remove, in one way or another, the B safety cap without great difficulty—many by using their teeth. At any rate, it must be realized that, regardless of what safety measures and precautions are taken, some children will circumvent them in any case.

Summary and Conclusions

A survey of 1,600 families has indicated that a safety closure of plastic is not only practical for manufacturers and mothers but also, if used on all packaged and prescribed medicaments, is a child-safety measure of real importance. The widespread adoption of a safety closure of some type for all drug containers in common home use could reduce in great part the morbidity and mortality from the accidental, experimental, and innocent ingestion of potentially poisonous drugs. Hospitals should lead the way in dispensing drugs only in bottles with a safety closure.

1410 Duke University Rd.

This study was supported by a grant from Plough, Incorporated, Memphis, Tenn.

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FORMALDEHYDE AS A FUMIGANT.—Disinfection by formaldehyde fumigation, unless it is to be inconveniently prolonged, has not the same margin of safety as disinfection by heat or chemical agents in solution. Formaldehyde should not, therefore, be used when any more certain method can conveniently be applied. We should not recommend it for any application where the killing of all pathogenic organisms is imperative, e.g. for surgical instruments, or the disinfection of the bedding of smallpox patients. The three applications for which formaldehyde seems most suitable are the disinfection of: (1) Rooms from which fabrics have been removed. A gas or vapor is commonly the only possible agent for this purpose. (2) Small objects which cannot be heated or wetted without damage, such as respirators, leather goods, boots, and toys not made of fabric. (3) Mattresses and woolen blankets. If these are spread out to allow access of the gas, surface disinfection is possible at room temperature, but if disinfection of the interior of the mattress or of folded blankets is required, some form of heated chamber must be used. —The Practical Aspects of Formaldehyde Fumigation, *Monthly Bulletin of the Ministry of Health,* December, 1958.

ILEAL INTUSSUSCEPTION AS RESULT OF INTESTINAL INTUBATION

Maxwell H. Poppel, M.D.
and
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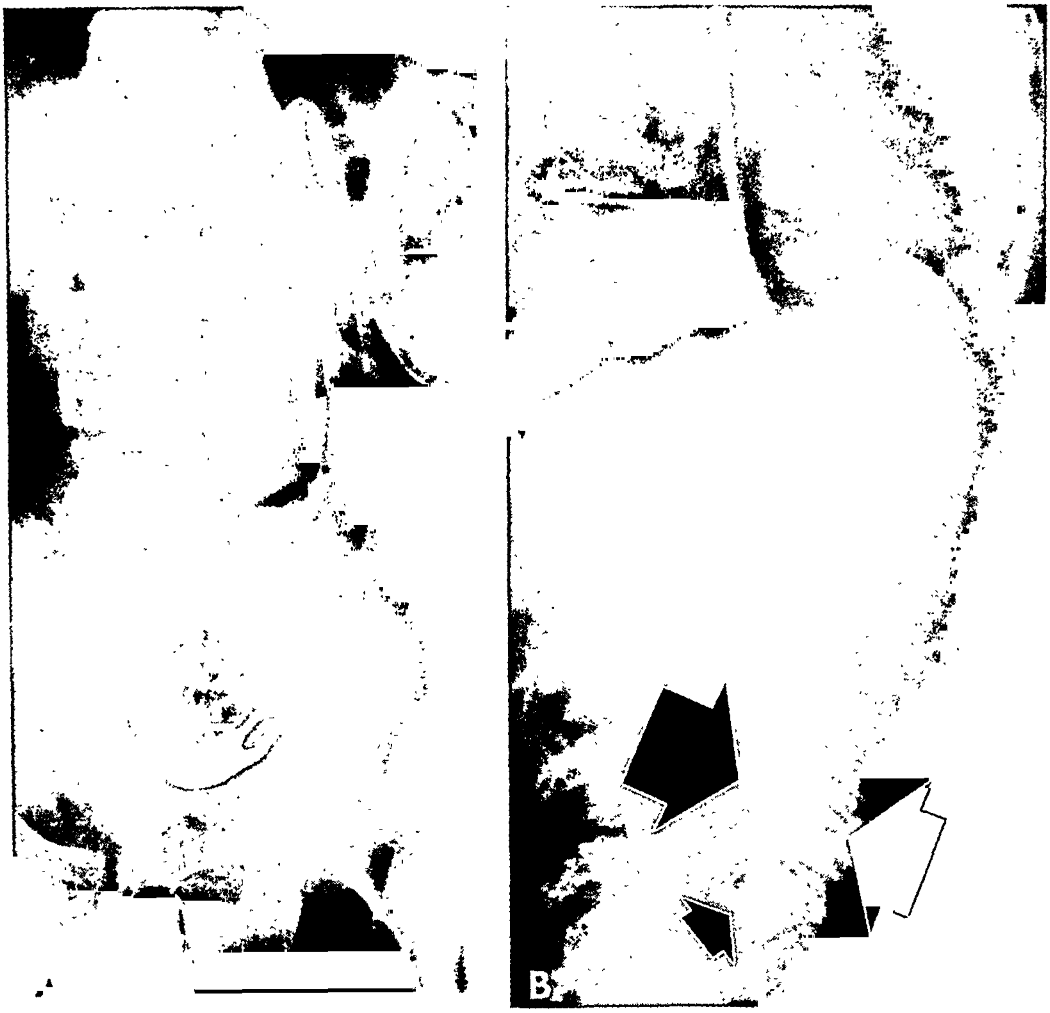
The long intestinal tube commonly employed in a wide variety of conditions has been in use for about 20 years. The single lumen tube was introduced in 1944, at which time mercury began to replace air in the tube's bag.[1] The complications of intubation have been discussed by many authors. The particular one reported in this paper is rare. Smith,[2] reporting on 1,000 intubations, failed to observe a single case of intussusception. Nichols,[1] using the Harris tube, had one case. Dunn and Shearburn [3] quote three cases from the literature and add one case of their own. Wangensteen [4] and Cantor and Reynolds [5] mention the long intestinal tube as a rare cause of intussusception.



A, mercury bag at site of obstruction before administration of diatrizoate. *B*, left lateral view with diatrizoate showing mercury-filled bag as part of intussusceptum (*small arrow*) and widened loop of ileum distal, but located above, acting as intussuscipiens (*large arrows*).

Recently such a complication occurred in one of our patients. We are reporting this case because it clearly visualizes the cause and effect and, to our knowledge, possesses the best illustrations of its kind.

Report of a Case

A 50-year-old man was first admitted in September, 1958, with a presenting complaint of abdominal pain of three days' duration. His history included a duodenal ulcer of 10 years' duration and partial gastrectomy 4 years prior to admission. Since then he had had intermittent abdominal pain. Three days prior to admission he experienced continuous left lower quadrant pain with vomiting of bile-stained fluid. He had fever and leukocytosis. A diagnosis of small intestinal obstruction was made and laparotomy performed the same day. Findings at operation were negative, even though special attention was directed to the entire small intestine.

From the Department of Radiology of the New York University–Bellevue Medical Center.

The postoperative course was uneventful until the ninth day, when the patient complained of abdominal cramps. Abdominal roentgenography revealed small intestinal distention with fluid-filled loops. Decompression of the intestine with a Cantor tube was attempted for four days. Diatrizoate (Hypaque) sodium study through the tube then revealed a complete obstruction in the ileum, with the mercury bag impacted at this site (see figure).

The roentgenologic findings indicated intussusception. The loop containing the mercury bag acted as part of the intussusceptum, while the small intestine loop just beyond was widened and acted as the intussuscipiens.

Immediately after the diatrizoate study he was reoperated on and an ileo-ileo-ileal intussusception was found and reduced, and the involved segment was resected. No significant gross abnormality was noted. The postoperative course was uneventful. The patient was discharged on the 13th postoperative day. Biopsy of the removed ileal segment revealed submucosal edema.

Wangensteen[4] reports intussusception as accounting for 0.4% of all cases of intestinal obstruction. The rarity of intussusception, especially in adults, may be appreciated from the statistics quoted by de Cesare[6]: of 113,351 hospital admissions in Duluth, Minn., there were 22 cases of intussusception but only 1 was in an adult; in 529,897 admissions to the Massachusetts General Hospital, from 1887 to 1946, there were 146 cases of intussusception, of which 43 were in adults.

Deterling and others[7] reported 40 cases of intussusception in adults. In five cases there was evidence that the intussusception was caused by the presence or withdrawal of a long intestinal tube. The clinical and x-ray features that they found most reliable were (1) obstruction to the free flow of barium, (2) marked narrowing of the valvulae at the site of obstruction, (3) gradual narrowing of the lumen proximal to the lesion, (4) local widening of the intestine with semicircular mucosal markings (concentric ring or spiral sheath), (5) palpable mass at the site of obstruction, and (6) changes in position and shape after defecation. In our case findings the first three features were present.

The vast majority of intussusceptions occur in infants, but a small number (5%) occur in adults. In contradistinction to most cases in children, an immediate cause for the intussusception is usually found in the adults, such as tumors or other pathological states of the intestine or its attachments. Among the rarest is an intussusception caused by foreign body or intestinal decompression tube. A search of the American literature reveals only 11 previous case reports involving a tube. The exact mechanism by which a tube causes intussusception is not clearly understood. Harris[8] believed that the distended balloon acted like a polyp, which was also the opinion of Dunn and Shearburn[3] and Cantor and Reynolds.[5]

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HYPERCORTISONISM IN PATIENTS WITH RHEUMATOID ARTHRITIS. —The clinical features of Cushing's syndrome which may be produced in patients receiving adrenal steroids are now familiar to most physicians. These features include fluid retention, moon face, abdominal striae, enlarged supraclavicular and cervicodorsal fat pads, hypertension, diabetes, osteoporosis, purpura, insomnia, hirsutism, excessive appetite, nervous tension, and other symptoms. It has been reported that from 66 to 75 per cent of all patients treated with adrenal steroids will develop one or more of these features. In addition to these usual features, however, many patients with rheumatoid arthritis under long term adrenal steroid therapy have been seen to develop certain unusual or "special" features of hypercortisonism. These special features comprise a syndrome which is characterized by musculoskeletal aching, fatigability, and cyclic mood changes. . . . Furthermore, these patients seem susceptible to so-called "mesenchymal reactions" which may simulate lupus erythematosus, a flare of rheumatoid arthritis, or periarteritis nodosa. Treatment of these special features of hypercortisonism consists in the steady, gradual reduction of dosage in small decrements according to the patient's reaction to the withdrawal.—J. W. Kemper, M.D., Hypercortisonism in Patients with Rheumatoid Arthritis, *Texas State Journal of Medicine,* December, 1958.

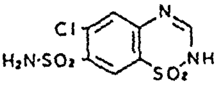
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Chlorothiazide (Diuril).—6-Chloro-7-sulfamyl-1,-2,4-benzothiadiazine-1,1-dioxide. — The structural formula of chlorothiazide may be represented as follows:



Actions and Uses.—Chlorothiazide, introduced commercially in 1958, is a potent, orally effective, nonmercurial diuretic agent. The drug is a potent inhibitor of the renal tubular reabsorption of sodium. In appropriate doses, it causes only a slight increase in excretion of bicarbonate and a considerable increase in the excretion of chloride. Potassium excretion is also increased but to a lesser extent than that of sodium or chloride. Under ordinary conditions of use, chlorothiazide does not alter urinary pH, nor does it cause significant changes in systemic acid-base balance. Its diuretic potency is greater than that of any other orally given nonmercurial diuretic presently available; it is only slightly less effective than parenterally administered mercurials. The mode of action of chlorothiazide in influencing the excretion of sodium and chloride has not been fully defined. Bicarbonate excretion is possible in the lower dose range because of a mild carbonic anhydrase inhibitory effect, but this effect is not responsible for the major excretion of sodium and chloride.

Chlorothiazide is rapidly and uniformly absorbed from the gastrointestinal tract. Its onset of action is rapid; diuretic effects are apparent within 2 hours after oral administration and persist for about 6 to 12 hours. Refractoriness to the drug is relatively uncommon even after prolonged periods of continuous administration.

Chlorothiazide is valuable as an adjunct in the management of congestive heart failure. The drug may be used for the initiation of diuresis as well as for the maintenance of the edema-free state in all types and degrees of severity of cardiac decompensation in which diuresis is required. As with any diuretic, patients with the most severe forms of the disease may be unresponsive to its action, particularly when the glomerular filtration rate is markedly reduced. Chlorothiazide is a satisfactory replacement for other orally given diuretics and can often be used in place of the parenterally administered organic mercurials. Its continued effectiveness makes it useful in many patients either who fail to respond or who have become refractory to other diuretics. Whereas therapy with chlorothiazide is not intended as a replacement for low-salt diets, administration of the drug makes it desirable to liberalize the salt intake in certain patients with congestive heart failure.

Chlorothiazide has been used with good results in the management of edema associated with nephrosis and certain types of nephritis. The drug may be of particular benefit to patients with nephrotic edema to whom corticotropin, glucocorticoids, and other agents which cause sodium retention are being administered concomitantly. If diuretic therapy is indicated in patients with edema caused by renal disease, chlorothiazide has an advantage over acetazolamide or ethoxzolamide in that it is most unlikely to precipitate a metabolic acidosis.

Chlorothiazide has been of value for the management of edema associated with liver disease, particularly portal cirrhosis. The drug has also been used for the treatment of toxemia and edema of pregnancy, for obesity or for premenstrual discomfort associated with fluid retention, and for the edema induced by such agents as corticotropin, adrenal cortical steroids, and certain estrogens.

In addition to its employment as a diuretic, chlorothiazide also is useful as an adjunct in the management of hypertension. When given alone, the drug generally has negligible or minimal lowering effects on the blood pressure. However, it is apparently capable of enhancing the effects of other antihypertensive agents such as Rauwolfia and Veratrum alkaloids, hydralazine, and the ganglionic blocking agents. It may also enhance the hypotensive effects of surgical sympathectomy. The mechanism of action of chlorothiazide in reducing high blood pressure has not been determined. The judicious use of chlorothiazide may make possible a sustained antihypertensive effect while allowing somewhat less rigid restrictions on dietary salt intake. When chlorothiazide is given in combination with other antihypertensive drugs, the dosage of the latter agents (particularly the ganglionic blocking agents and hydralazine) must be reduced markedly; this decreases or even eliminates certain of the more troublesome side-effects, including those resulting from parasympathetic ganglionic blockade.

Chlorothiazide is apparently well tolerated, and few serious immediate side-effects have been reported to date. It should be borne in mind, however, that the drug is an extremely potent compound in its influence on fluid and electrolyte excretion. It should not be given unless the patient can be regularly and carefully observed for the early signs of fluid and electrolyte imbalance and unless appropriate measures can be taken to prevent such imbalance or to correct it if it occurs.

In some patients, chlorothiazide may produce a hypochloremic alkalosis as the result of excessive excretion of chloride in relation to sodium and a concomitant rise in plasma bicarbonate levels. In these cases, the excretion of potassium is also likely to be excessive so that a hypokalemia is superimposed on the hypochloremic alkalosis. These electrolyte imbalances are more likely to occur during excessive or continued administration of the drug to patients who either fail to show a natriuretic response or, having shown an initial response, do not continue this response. Hypokalemia may result in increased sensitivity to the action of digitalis. Caution must therefore be employed to prevent hypokalemia when digitalis is administered. Changes in the dosage requirements for both digitalis and chlorothiazide must be anticipated. Patients with myocardial ischemia as a result of coronary artery disease may also have a predisposition to serious cardiac arrhythmias if hypokalemia occurs. Hypochloremic alkalosis may be treated by making up the chloride deficiency (ammonium chloride should not be given to patients with hepatic disease). Hypokalemia should be corrected by giving potassium chloride. Both electrolyte disturbances can usually be reversed by the temporary discontinuance of chlorothiazide.

Occasionally the so-called low-salt syndrome may complicate therapy with chlorothiazide in patients with severe congestive heart failure who are markedly edematous. This complication is most likely to occur when excessive amounts of the drug are administered at the same time that dietary salt intake is rigidly restricted. In some cases, it may be necessary to treat this condition with the cautious infusion of hypertonic sodium chloride solutions along with rigid restriction in water intake, even in the presence of intense thirst.

In patients with severe renal or hepatic impairment, as indicated by clinical and laboratory observations, diuretic therapy may be ineffective and even contraindicated.

In patients with advanced cirrhosis, chlorothiazide should be administered cautiously; it may be necessary in some instances to discontinue administration. It should be borne in mind that in certain patients with hepatic disease, particularly those who have a history of a previous episode of hepatic coma or precoma, electrolyte imbalance (among other factors) may precipitate hepatic coma. When chlorothiazide is used in patients with cirrhosis, it may be desirable to place them on a low-protein diet and to administer potassium glutamate by mouth, as well as a broad-spectrum, nonabsorbable antibiotic such as neomycin, to minimize the possibility of coma.

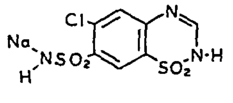
Rare side-reactions to chlorothiazide include nausea, epigastric discomfort, dizziness, weakness, and paresthesias. In occasional instances, a drug rash has been observed. The possibility of allergic reactions arising from sensitivity to the drug should be borne in mind.

Dosage.—Chlorothiazide is administered orally. Dosage must be highly individualized according to the response of the individual patient and the severity of the condition being treated. For diuretic effects, the usual dose for adults ranges from 500 mg. to 1 Gm. once or twice a day. A total daily dose of 1 Gm. or more is usually given in two divided doses. For antihypertensive effects in conjunction with the use of other antihypertensive drugs, the dosage of chlorothiazide ranges from as little as 250 mg. twice daily to 500 mg. three times a day.

Preparations: tablets 250 mg. and 500 mg.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorothiazide.

Chlorothiazide Sodium (Lyovac Diuril).—The sodium salt of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide.—The structural formula of chlorothiazide sodium may be represented as follows:



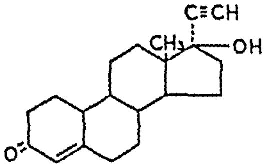
Actions and Uses.—The sodium salt of chlorothiazide, introduced commercially in 1958, has the same actions and uses as the parent substance except that it is more soluble and therefore suitable for parenteral injection. (See the monograph on chlorothiazide.)

Dosage.—Chlorothiazide sodium is administered intravenously. The lyophilized powder is reconstituted with a suitable volume of sterile diluent immediately prior to administration. The drug may be given as a concentrated solution by direct intravenous injection or may be infused slowly by intravenous drip. Dosage is the same as for chlorothiazide.

Preparations: powder (injection) 500 mg.

Merck Sharp & Dohme, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of chlorothiazide sodium.

Norethindrone (Norlutin). — 17α-Ethinyl-19-nortestosterone.—The structural formula of norethindrone may be represented as follows:



Actions and Uses.—Norethindrone, sometimes referred to as norethisterone, is a highly potent, orally active, progestational agent which was introduced commercially in 1957. It produces the typical physiological and anatomic effects of progesterone and its derivatives, i. e., induction of a secretory endometrium, luteal changes in the vaginal epithelium, disappearance of cervical fern, increases in basal body temperature, and withdrawal bleeding from an estrogen-primed endometrium. When given from the 5th to the 25th day of the menstrual cycle, the drug is believed to inhibit ovulation. Continuous administration of norethindrone can also delay menstruation for prolonged periods, with only occasional instances of breakthrough bleeding. The pseudopregnancy thus induced is presumably an anovulatory amenorrhea. In terms of weight of drug required for progestational effects, norethindrone is one of the most potent agents known. Its onset and duration of action are about the same as with parenterally administered progesterone; if given for five days to amenorrheic women after estrogenic stimulation, the drug will generally induce withdrawal bleeding within 24 to 72 hours after its discontinuance. Animal experiments indicate that norethindrone has slight estrogenic effects; there is no evidence of androgenic activity. However, studies in animals are not adequate to estimate the extent to which observed histological changes may be due to the estrogenic activity of the drug. The drug is apparently not metabolized in the same manner as progesterone, since its administration does not cause an increase in the urinary excretion of 17-ketosteroids.

Norethindrone has been used in the treatment of primary and secondary amenorrhea. The drug will not induce secretory changes in the endometrium, with subsequent menstruation, unless there has been adequate estrogenic stimulation. Hence, in patients with inadequate endogenous estrogen production, as determined by vaginal cytology, estrogen priming is necessary. In women with menstrual irregularity or secondary amenorrhea due to inadequate corpus luteum activity, the monthly employment of norethindrone may help in reestablishing a normal cyclic pattern. This effect may be helpful in the management of patients with infertility problems, since it permits a more accurate prediction of the time of ovulation. Although the ultimate value of progestogens in the treatment of female infertility remains to be determined, agents such as norethindrone might theoretically be of value in establishing conditions conducive to pregnancy by reason of their inhibiting effect on the arborization of cervical mucus (which may act as a barrier to sperm penetration) and by preparing the endometrium for implantation of the ovum. Like other progestogens, norethindrone may be tried in the treatment of functional uterine bleeding, provided that genital malignancy has been ruled out and that curettage has established the diagnosis of benign endometrial hyperplasia.

Because it can induce a state of amenorrhea for as long as its daily administration is continued, norethindrone has been suggested as a means of temporary delay of the menstrual period for honeymoon, vacation, and athletic events. However, the use of a potent hormone to inhibit a normal physiological function, simply for patient convenience, should be discouraged. The menstrual-inhibiting property of the drug may, however, serve a useful purpose in alleviating the symptoms of endometriosis and causing a regression of endometrial implants.

Norethindrone, as well as other progestogens, has been tried in a more or less empirical manner for the treatment of threatened or habitual abortion. At present, there is a dearth of convincing evidence that any agent of this type can reduce the incidence of fetal loss. There is likewise insufficient evidence at hand to establish the proposed use of norethindrone for the treatment of premenstrual tension or dysmenorrhea.

The clinical use of norethindrone has not been associated with any appreciable toxicity. In occasional instances, mild nausea, lethargy, and spotting before the calculated onset or after termination of menstruation have been reported. In young animals, prolonged administration of large doses of the drug causes a decrease in food consumption, with a consequent depression in weight gain; however, anorexia and weight loss have not been a problem clinically. Prolonged therapy with norethindrone generally decreases libido, an effect that would negate its proposed use to delay menstruation during the honeymoon.

Dosage.—Norethindrone is administered orally. For amenorrhea, menstrual irregularity, functional uterine bleeding, and infertility, the usual dose is 10 to 20 mg. daily from the 5th to the 23rd day of the menstrual cycle. A five-day period is allowed for withdrawal bleeding to occur. Continuous daily doses of 20 to 30 mg. are usually sufficient to prevent menstruation. For the treatment of premenstrual tension and dysmenorrhea, the proposed dose is 10 mg. once or twice daily, beginning in the preovulatory phase and continuing to the 20th to the 23rd day of the cycle. Pending more evidence to show a beneficial effect, the proposed dosage for these latter purposes is considered experimental.

Preparations: tablets 5 mg.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of norethindrone.

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ABUSE OF ANTIBIOTIC LOZENGES

ELSEWHERE IN this issue of THE JOURNAL (page 1235) a correspondent directs attention to the development of moniliasis of the soft palate and pharynx, sometimes fatal, after the use of antibiotic lozenges. Although antibiotic lozenges enjoy a degree of popularity in the local treatment of diseases of the throat, it is known that effective concentration of the contained medication cannot be maintained for long periods on the surface of the tonsils or pharynx because of the continual washing effect of saliva. There is no such response as rendering the throat sterile, or even antiseptic, except possibly for a short time.

In superficial infections of the throat, local administration of antibiotic and chemotherapeutic agents may be effective. However, their value diminishes if the micro-organisms have penetrated into the tissues. Actually, once micro-organisms have established themselves below the surface, and an abscess has formed, locally applied medicaments have little value. In acute streptococcic tonsillitis, for example, all of the offending organisms are not found on the surface of the tonsils—in reality, many of them lie deep in the tonsillar tissues. Under such circumstances, the value of lozenges, troches, pastilles, and medicated chewing gum is dubious. Deeply seated bacteria are best approached systemically. It is dangerous to rely on local medication alone in the treatment of severe infections of the throat.[1]

Inadequate dosage and indiscriminate usage of topical antibiotic and sulfonamide compounds in the treatment of infectious diseases of the throat can breed resistant bacterial strains. Their promiscuous use is unwarranted in trivial infections; moreover, their use is limited from time to time by the development of allergic reactions, by the sensitiveness of patients to these agents, by the acquisition of antibiotic-resistance and sulfonamide-resistance states, and by their ability to mask symptoms occasionally. Finally, stomatitis has been traced to various antibiotics and sulfonamides present in a variety of lozenges, troches, pastilles, and medicated chewing gum.

---

[1] Fabricant, N. D.: Modern Medication of Ear, Nose and Throat, New York, Grune & Stratton, Inc., 1951.

THE PHYSICIAN'S ROLE IN SAFE DRIVING

In this issue of THE JOURNAL, *page 1195, is a* report prepared by the Committee on Medical Aspects of Automobile Injuries and Deaths which will be of value to physicians called on to advise whether or not an individual is capable of driving a motor vehicle safely.

It can easily be determined if the individual meets the physical standards for driver licensing established by the state licensing authority. These standards lend themselves to precise measurement. Not easily measured and not well understood in the production of automobile accidents are factors such as poor judgment, emotional disturbances, and faulty attitudes.

Injuries suffered in automobile accidents are an important health problem in the United States. About 37,000 persons were killed in automobile accidents in 1958 and about 5 million were injured seriously enough to require medical attendance or restriction of their activity for one day or longer.

Most automobile accidents occur because of human failures. Many drivers are physically, mentally, emotionally, or physiologically impaired, sometimes only temporarily, sometimes permanently. The evaluation of impairment in relation to safe driving ability is best done by physicians. It is the purpose of the guide, which this committee prepared after some two years of study, to assist the physician in his evaluation.

The number of registered vehicles, the number of licensed drivers, and the number of miles driven are steadily increasing. Exposure to motor vehicles occurs daily in the lives of the majority of Americans. The many groups working in the accident prevention field are trying to see that this exposure does not result in injury. Physicians can make a great contribution in automobile accident prevention by determining the fitness of drivers to operate motor vehicles.

ORGANIZATION SECTION

MEDICAL GUIDE FOR PHYSICIANS IN DETERMINING FITNESS TO DRIVE A MOTOR VEHICLE

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Introduction

Traffic accidents killed about 37,000 individuals in 1958 and injured about 1,350,000, according to the National Safety Council. These data were developed from the reports of official agencies. The data refer to the number of injuries causing disability beyond the day of the accident. The U. S. Public Health Service has estimated that there are about 4,700,000 injuries annually in automobile accidents. This estimate was based on the National Health Survey of 1957-1958 which derived its data from household interviews. Persons with injuries involving one or more days of restricted activity or medical attendance were included. On the basis of the latter figure it has been predicted that 1 person in every 10 in this country will be injured or killed in a motor vehicle accident within the next four years. This constitutes one of the nation's largest unsolved health hazards.

It is the purpose of this guide to call attention to the areas in which the medical profession may be of help in combating this serious health problem. This guide has been prepared to assist physicians in examining patients and advising them on their ability to operate a motor vehicle safely. Physical, mental, and emotional states or disabilities likely to impair driving ability are specifically enumerated along with the problems of temporary incapacities from medicaments and alcohol.

The physical and mental demands of the task of driving vary greatly with the type of vehicle and the type of driving. For this report, three types of vehicles have been considered—the private motor vehicle, the commercial vehicle, and the passenger transport vehicle. The driver of the commercial or passenger transport vehicle cannot usually choose the hours he will drive nor the route he will take. The driver of the private vehicle may, in many cases, select both the time of his travel and the route. The driver of the commercial or passenger transport vehicle will spend more hours daily in driving than most drivers of private vehicles. There is little similarity between the demands on the resources of the individual who drives half a mile to the store on a rural road with no intersections and the individual who drives in rush hour traffic in a metropolitan area. The physician should keep these matters in mind when advising his patients on their fitness to drive.

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All states but one have laws concerning the physical requirements for driver licensing. Every physician should be familiar with the laws, and his advice to patients must be consistent with the laws of the state in which his patient is licensed.

Human failure overshadows all other factors in the production of highway accidents. The human mechanism must be in good condition to cope with the split second timing needed to maneuver responsive high speed motor vehicles. There is no doubt that poor judgment, impaired reaction time, faulty attitudes, emotional disturbances, and physical disabilities, including impairment of the sensory organs, are basically responsible for most accidents. Thus, the key to ultimate success in automobile accident prevention lies in the driver—his intelligence, his sense of personal and social responsibility, his reactions to various stimuli in normal conditions and under stress, and his driving ability in good health and in illness.

The physician is qualified by training to ascertain the physical, mental, emotional, or physiological impairments of an individual. Moreover, he is in a good position to evaluate these impairments in relation to safe driving ability. Obviously, it is not always easy to arrive at a decision in these cases. Variations in severity of illness or impairment, variations in individual reactions and adjustment, and variations in individual response to medicaments are significant factors in evaluating each case. However, even in the realm of behavior patterns, the physician is in an ideal position to do effective counseling by translating scientific data into terms of lay understanding. Few patients realize the small amounts of alcohol required to impair dangerously their driving ability or that alcohol is involved in about 50% of automobile accidents with fatalities; nor does the slightly inebriated driver realize that he materially increases his likelihood of a serious accident.

A conscientious individual may inquire, "Doctor, is it all right for me to drive an automobile in my condition?" This situation usually is conducive to a receptive patient attitude if perchance the advice may be "bad news." Frequently, it may be necessary for an equally conscientious physician, recognizing his responsibility for the safety of his patient and the public, to caution the patient against driving for a certain period of time or even permanently, unhappy as this may make the patient. Many of these conditions have been graphically described for the lay public in a previous publication of this Committee, entitled "Are You Fit to Drive?" Physicians should find this descriptive pamphlet (available from the Association of Casualty and Surety Companies, 60 John St., New York 38) helpful in dealing with adamant patients.

When physicians discover any conditions in their patients which might make it inadvisable for them to drive a motor vehicle, they should advise the patients to report the condition on the next application for renewal of the driver's license. This is for the patient's own protection. If this information is not reported on the application and the applicant subsequently becomes involved in an accident to which the condition either directly or indirectly might be a contributing cause, in many states the insurance company may legally refuse liability.

This guide is devoted to the physician's role in helping prevent motor vehicle accidents through appropriate advice and treatment to patients. However, it is recognized that many accidents will continue to occur. Therefore, the Committee also is interested in preventing, as much as possible, personal injury to the occupants of vehicles involved in accidents.

The elimination of many road hazards by improved highway design and construction is proceeding at a fast pace. Also, there has been great improvement in the maneuverability, responsiveness, and speed of acceleration and deceleration of automobiles. In the construction of the motor vehicle lies a great opportunity for the prevention of serious injury to the occupants when accidents do occur. It is possible to design, build, and equip an automobile so that injury or death will occur only in the more extreme crashes. In a car so designed and equipped, personal injuries and deaths would be minimized although accidents continue to occur. It is obviously simpler mechanically to change the design of automobiles to protect frail man than it is biologically to change the design of man to resist traumas—therefore the present urgency for automotive engineers to lend their great talents to this end. Of course, the public needs to understand, accept, and be willing to pay for such design and mechanical changes.

It is probable that the next decade will see a greatly increased emphasis upon more stringent physical standards for driver licensing. It is believed that more and more patients will turn to their physicians for advice and assistance in this regard. In a subsequent publication, this Committee will recommend physical standards for driver licensing and for the guidance of licensing authorities and physicians.

Medicine

Fever, fatigue, metabolic diseases, effects from various drugs, and carbon monoxide poisoning are among the medical conditions adversely affecting driving ability. Cardiovascular disease and alcohol are dealt with in separate sections. Physicians should be familiar with the entities here described.

Assessing Safe Driving Ability.—In general, the individual should be assessed medically to determine the answers to the following questions: 1. Has the patient the physical and mental ability to manipulate the controls? 2. Is the patient likely to suffer excessive fatigue that will impair his driving ability? 3. Does the patient have the required vision and hearing for safe driving? 4. Has the patient any physical or mental disorder likely to cause confusion or a sudden loss of consciousness while driving? 5. Is the patient likely to suffer a temporary impairment of mental, physical, or functional capacity due to alcohol, drugs, infections, or medical treatment, etc., making it unsafe for him to drive? 6. Does the patient have good emotional control or has he signs of antisocial behavior or an emotional disturbance making it unsafe for him to drive?

Metabolic Diseases.—Disturbances in function of the endocrine glands cause many varied symptoms from generalized asthenia, muscle weakness, and spasm or tetany to sudden episodes of vertigo or unconsciousness. Individuals so afflicted should be advised not to drive a motor vehicle until these symptoms have been controlled by appropriate therapy. The more important conditions likely to impair the driving ability of such patients are discussed briefly:

Diabetes Mellitus: Patients suffering from diabetes mellitus of a degree that can be controlled adequately by diet alone may drive any type motor vehicle. Also older individuals with mild diabetes controlled by diet and a sulfonylurea type drug who experience no reactions from the drug may drive any type motor vehicle. If insulin is required and the diabetes well controlled, the individual may drive a private vehicle. However, he should be advised not to drive a commercial or passenger transport vehicle because of the possibility of a sudden attack of hypoglycemia. The uncontrolled diabetic should be advised not to drive any type motor vehicle because of the development of disabling complications. On the other hand, an individual with true renal glycosuria may safely drive any type motor vehicle.

Hyperinsulin States: Individuals suffering from recurring spontaneous attacks of hypoglycemia, pancreatic islet cell adenoma, or other organic or functional causes should be advised not to drive any type of motor vehicle while subject to an attack of faintness, giddiness, or unconsciousness. Patients with mild cases who never develop unconsciousness or disabling symptoms of faintness may drive a private vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Thyroid Disease: In addition to having tachycardia, exophthalmos, and tremor, patients with hyperthyroidism are prone to emotional disturbances, anxiety, and even psychotic symptoms. Therefore, individuals with thyrotoxicosis should be advised not to drive any type of motor vehicle until the disabling symptoms are well controlled. In addition, individuals suffering from an enlarged thyroid gland with pressure symptoms should be advised not to drive a commercial or passenger transport vehicle, although usually they can drive a private vehicle. Individuals with marked myxedema or cretinism should be advised not to drive a motor vehicle.

Hyperparathyroidism and Hypoparathyroidism: Individuals suffering from hyperparathyroidism with muscular weakness and hypotonia should be advised not to drive a motor vehicle. When symptoms are mild or well controlled by therapy, these individuals may drive private motor vehicles but not commercial or passenger transport vehicles.

Individuals suffering from acute hypoparathyroidism with increased neuromuscular excitability, cramps, spasm, and generalized tetany should be advised not to drive a motor vehicle. Chronic hypoparathyroidism varies greatly in its manifestations and severity. Persons with mild cases without tetany may drive private motor vehicles but should be advised not to drive commercial or passenger transport vehicles. However, with the development of tetany, muscular weakness, or ease of fatigue, these patients should be advised not to drive any motor vehicle.

Posterior Pituitary Insufficiency: Individuals suffering from diabetes insipidus should be advised not to drive a commercial or passenger transport vehicle. Under careful medical supervision they may drive private motor vehicles unless visual disturbances or other disabling central nervous system symptoms develop.

Anterior Pituitary Insufficiency: The severe carbohydrate deficiency and spontaneous hypoglycemic episodes that characterize hypopituitary cachexia (Simmond's disease) make it mandatory that these individuals should not drive any motor vehicle. Under close medical supervision, those persons making a good recovery and without hypoglycemic episodes may drive a private motor vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Acromegaly: With the development of muscular weakness and pain, ease of fatigue, cardiac enlargement, and intractable headaches, patients with acromegaly, or gigantism, should be advised not to drive any motor vehicle. Moreover, about 50% of these patients develop visual disturbances which also make it unsafe for them to drive.

Adrenal Cortical Hyperfunction: Patients with adrenal cortical hyperfunction (Cushing's disease), who develop muscular weakness and osteoporosis, should be advised not to drive a motor vehicle. Good recovery after appropriate therapy enables these individuals again to drive a private vehicle. However, they should be advised not to drive a commercial or passenger transport vehicle.

Adrenal Cortical Hypofunction: Patients with well-developed cases of adrenal cortical hypofunction (Addison's disease), particularly those with asthenia and/or persistent low blood pressure, should be advised not to drive a motor vehicle.

Persons with mild cases or those whose symptoms of asthenia and low blood pressure are well controlled by therapy may drive a private vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Hyperfunction of Adrenal Medulla: Hyperfunction of adrenal medulla occurs with the development of pheochromocytoma tumor which clinically is characterized by attacks of headache, dizziness, weakness, and blurring of vision with a rapid pulse and elevated blood pressure. Until completely free of these attacks by removal of the tumor, such individuals should be advised not to drive a motor vehicle.

Drugs.—Numerous drugs, either self-administered or taken at the direction of a physician, produce reactions in some individuals impairing that individual's ability to drive a motor vehicle. The degree of impairment varies tremendously, depending on the severity and type of reaction. Physicians administering drugs likely to produce reactions impairing sensory, mental, or physical functions have a clear responsibility to fully inform their patients concerning this matter, especially as it effects their ability to drive a motor vehicle.

In addition, some patients experience unusual reactions to drugs that ordinarily do not produce disabling symptoms. Physicians must ever be alert to this possibility. Should unusual reactions, allergic or otherwise, occur which impair sensory, mental, or physical functions making it unsafe to drive, the physician must advise the patient not to drive a motor vehicle until the disabling symptoms have been eliminated. The more important groups of drugs likely to impair driving ability are discussed briefly.

Central Nervous System Depressants: The drowsiness induced by analgesic drugs sufficiently impairs driving ability so that patients with such drowsiness should be advised not to drive a motor vehicle. In addition, morphine, its derivatives, and the synthetic narcotics, such as meperidine (Demerol) hydrochloride, cause varying amounts of euphoria, inability to concentrate, apathy, dimness of vision, and rapid flow of uncontrolled thought. Patients under the influence of these drugs should be advised not to drive a motor vehicle.

Hypnotics, Sedatives, and Anesthetics: Hypnotics, sedatives, and anesthetics not only depress central nervous system activity, producing drowsiness and sleep, but also they may produce motor and sensory changes. No doubt small doses of some of these drugs, quieting a highly excited and "jittery" patient, may actually temporarily improve his driving ability. However, this is not the usual circumstance. Therefore, it is best to advise patients taking hypnotic doses of these drugs not to drive a motor vehicle. Patients receiving mild sedation who experience no drowsiness may drive. Of course, a barbiturate addict is incapable of driving a motor vehicle safely. Patients receiving barbiturates and local anesthetics for minor surgery should be advised not to drive.

Tranquilizing Drugs: During the initial period of administration of tranquilizing drugs, such as meprobromate, chlorpromazine, and reserpine, some drowsiness is frequently experienced. Also, with large doses, the accompanying hypotension may occasionally produce short episodes of faintness or giddiness. Therefore, during the initial phase of dosage adjustment, the patient should be advised not to drive a motor vehicle if he is experiencing drowsiness or faintness. At all times these patients should be carefully observed for symptoms of drowsiness or faintness. Patients stabilized on a maintenance dosage of these drugs, who are without symptoms of drowsiness or episodes of faintness, may drive a private motor vehicle but should be advised not to drive a commercial or passenger transport vehicle.

Central Nervous System Stimulants: Although central nervous system stimulants, such as amphetamines, temporarily increase alertness and efficiency, large doses in some individuals may produce headache, dizziness, agitation, irritability, and a decreased ability to concentrate. In all individuals, a period of fatigue and depression follows the initial stimulation. In rare instances an individual may take one of these drugs to prolong the period of alert driving. The dosage should not be more than 5 or 10 mg. and without repetition that day. Drugs of this type should be used only on advice of a physician.

Antihistamines and Drugs Preventing Motion Sickness: There is great individual difference in reaction to antihistamines and drugs preventing motion sickness, with dizziness or drowsiness occurring fairly frequently. Moreover, it is unpredictable in which individuals these symptoms will occur. Patients under medication with these drugs should be advised not to drive a motor vehicle until it has been established by prior trial that they do not experience dizziness or drowsiness.

Anti-infective Agents: In full and prolonged dosage with anti-infective agents, there may occur undesirable reactions of nausea, loss of sense of balance with dizziness, ringing in the ears, and deafness. A patient developing such symptoms should be advised not to drive a motor vehicle. Patients receiving over 1 Gm. of streptomycin daily should be watched carefully for the development of adverse symptoms.

Sulfonamides: Patients receiving sulfonamides should be warned that if they develop any drowsiness or dizziness they at once should cease driving a motor vehicle.

Hallucinogens: Hallucinogens, such as marijuana, have singular abilities for changing normal emotional reactions even causing individuals to become oblivious or indifferent to their surroundings. Individuals under the influence of these drugs should be advised not to drive a motor vehicle.

Fatigue.—Fatigued, drowsy, and sleepy drivers are responsible for many accidents. They are unable to make split second decisions, reaction time is slowed, and there is loss of peripheral vision and attention. In addition, many individuals are victims of "highway hypnosis," or hallucinations, some after only a few miles of monotonous superhighway driving. Among commercial and passenger transport drivers, most accidents occur within a few hours after the start of a trip. This is due, in part, to their off-duty activities. Thus, all drivers should be cautioned against driving after inadequate rest. Moreover, persons who periodically develop "highway fatigue" should be advised against driving a commercial or passenger transport vehicle.

Because of the development of fatigue, patients should be advised not to drive over eight hours in one day. The vehicle should not be kept too warm, and on continuous drives the operator should be advised to stop, get out, and walk around every two or three hours. In some instances, despite partial fatigue, a driver must proceed. Caffeine in the form of coffee, cola drinks, or tablets will help some individuals. In the rare case where prolonged driving is necessary, a central nervous system stimulant such as benzedrine may be used, but physicians should be very cautious in prescribing stimulants for this use.

Fever and Infectious Diseases.—Patients in the fever stage of an infectious disease should be advised not to drive because of decreased attention and impaired judgment and reaction time.

Carbon Monoxide.—The adverse effect of carbon monoxide, from exhausts and from smoking, on driving ability is in decreasing the visual sensitivity of the eye in areas of low illumination. The relative oxygen deficiency from smoking three cigarettes is equal to that of traveling at a 7,500-ft. altitude. Since adequate ventilation does not take care of chain smokers who inhale, drivers should be advised to refrain from frequent smoking prior to and during periods of night driving or at high altitudes.

Cardiovascular Disease

The examination of the cardiovascular system in determining a patient's ability to drive a private, commercial, or passenger transport vehicle should consist of a complete cardiac history and physical examination. The history should establish presence or absence of edema, orthopnea, cyanosis, dyspnea, and substernal or precordial pain. Also, a history of rheumatic fever, congenital deformities, thyroid disease, syphilis, hypertension, and anemia should be sought.

In order that the cardiovascular system be properly evaluated, the entire body must be examined, including the fundi, lungs, abdomen, and extremities. The physical examination, including palpation, percussion, and auscultation of the heart, should determine if venous congestion, cardiac enlargement, or valvular disease is present. The heart rate, rhythm, and level of blood pressure should also be ascertained.

Urinalysis, blood count, sedimentation rate, and serologic tests for syphilis should be done. Cardiac fluoroscopy, chest x-ray, and an electrocardiogram complete the examination of the cardiovascular system. In evaluating the cardiac status of an individual, it is important to ascertain the presence of cardiovascular disease and then its status according to cause, anatomic defects, physiological abnormalities, and functional capacity.

The lack of conclusive statistical data concerning the role of each cardiac condition as a potential driving hazard is recognized. However, on the basis of knowledge of pathological physiology and the clinical course of these cardiac conditions, it is believed that a medical opinion can be formulated as to the potential driving hazard. These hazards include sudden death, lapse of consciousness, and pain sufficient to cause loss of control of the car.

Etiological and Anatomic Classification.—The principal disabling cardiac conditions and their significance in relation to the safe operation of a motor vehicle are portrayed. It is hoped that this material, presented on (1) an etiological and anatomic basis and (2) a physiological and functional capacity basis, may serve as a basic guide for physicians in their evaluation of such patients.

Rheumatic Fever: Any evidence of active rheumatic fever calls for marked restriction of activity. Therefore, such a patient should be advised not to operate a motor vehicle.

Rheumatic Heart Disease: Appraisal must be made of the extent of damage in connection with valvular deformity, derangements of rhythm, progressive cardiac enlargement, and myocardial insufficiency. Aortic stenosis, when marked, is prone to lead to angina pectoris, syncope, or sudden death. Patients with significant aortic stenosis should be advised not to operate a motor vehicle. Patients with lesser degrees of aortic stenosis without symptoms of angina or syncope should be advised not to operate passenger transport vehicles but may operate a commercial or a private motor vehicle. Patients with aortic insufficiency and left ventricular failure with dyspnea or paroxysmal nocturnal dyspnea should be advised not to operate a motor vehicle. Patients with lesser degrees of aortic insufficiency without dyspnea should be advised not to operate passenger transport vehicles but may operate a commercial or private motor vehicle.

Patients with myocardial insufficiency due to mitral stenosis or insufficiency should be advised not to operate either commercial or passenger transport vehicles but may continue to operate a private vehicle when the myocardial failure is well controlled by therapy with only minimal dyspnea on exertion. Valvular deformity due to rheumatic fever involving the tricuspid and pulmonic valves is less common. Patients with evidence of right-sided heart failure should be advised not to operate either commercial or passenger transport vehicles. If the heart failure is controlled by therapy, the patient may operate a private motor vehicle. A superimposed subacute bacterial endocarditis necessitates immediate treatment and abstinence from operating any motor vehicle.

Disturbances of rhythm are frequent complications of rheumatic heart disease. Uncontrolled auricular tachycardia, flutter, or fibrillation with a rapid ventricular rate is apt to be associated with a diminished cardiac output, severely incapacitating the patients, and therefore they should not operate any motor vehicle. However, when well-controlled by therapy, such patients may operate a motor vehicle. Because of the work load and stress on the heart and the danger of embolization, patients having auricular fibrillation should be advised not to operate commercial or passenger transport vehicles.

Hypertensive Cardiovascular Disease: The upper limit of normal blood pressure is considered to be 150-160/90 mm. Hg. Many patients have labile blood pressures and particularly when seen on the first examination in the office may show levels of pressure above this. If the blood pressure is consistently above 150-160/90 mm. Hg., fixed hypertension must be considered to be present and its cause should be ascertained. Hypertension in itself is not disabling for the safe operation of a motor vehicle, but the complications arising from hypertension, i. e., damage to brain, eyes, heart, or kidneys, may well prove to be so disabling. When the complications of hypertension are limited to the optic fundi, the degree of impairment of driving ability should be evaluated solely on the basis of loss of vision. If there is any evidence that the hypertension has caused cardiac damage resulting in congestive heart failure or angina pectoris, such patients should be advised not to operate a motor vehicle, unless the congestive failure or angina is well controlled by therapy.

Arteriosclerotic Heart Disease: Sclerosis of the coronary vessels results in diminution of blood flow, particularly during exertion, with insufficient nourishment of the myocardium, resulting in angina pectoris. If the original attacks are mild, infrequent, and controlled with therapy, such patients may still drive private motor vehicles but not commercial or passenger transport vehicles.

More prolonged episodes of inadequate myocardial nourishment and substernal pain are termed coronary insufficiency. Arteriosclerotic heart disease may also result in various abnormalities of conduction with varying degrees of heart block, ventricular premature contractions, or arrhythemias. Patients with such symptoms well controlled by therapy may drive private motor vehicles. They should not operate commercial or passenger transport vehicles.

Syphilitic Heart Disease: Patients with syphilitic aortitis having syncope, congestive heart failure, or angina pectoris should be advised not to operate a motor vehicle. If syphilitic aortitis has led to the development of aortic insufficiency, then careful evaluation should be made of the patient concerning the presence of angina pectoris, syncopal attacks, left ventricular enlargement, or congestive heart failure. If any of these have occurred, the patient should not operate commercial or passenger transport vehicles, and, unless the symptoms are well controlled by therapy, the patient should be advised not to operate a private motor vehicle.

Bacterial Endocarditis or Endarteritis: Patients with acute bacterial endocarditis under vigorous treatment are so ill and their activities so restricted that they should not consider operating a motor vehicle. In addition, patients with subacute bacterial endocarditis, because of the danger of embolization to the brain, should be advised not to operate a motor vehicle.

Metabolic Heart Diseases: Patient with thyrotoxic or beriberi heart disease or with severe anemia with impairment of oxygenation of the myocardium or myxedema heart disease, when severely ill, are so incapacitated that they should be advised not to operate a motor vehicle.

Congenital Heart Disease: Some cases of congenital heart disease, such as patent ductus arteriosus, coarctation of the aorta, tetrology of Fallot, and septal defects are amenable to surgical treatment. If signs of myocardial insufficiency are present, such patients should be advised not to operate a commercial or passenger transport vehicle but may operate a private vehicle unless symptoms of myocardial insufficiency are pronounced. Asymptomatic congenital heart lesions are of no significance.

Cor Pulmonale: Patients with right-sided heart failure secondary to disease of the lungs with venous distention, enlargement of the liver, ascites, and edema should be advised not to operate commercial or passenger transport vehicles. However, if the symptoms of right ventricular failure are mild and well controlled by therapy, such patients may operate private motor vehicles.

Myocarditis: Any evidence of active myocarditis due to rheumatic fever, diphtheria, or other causes requires bed rest, and such patients should therefore be advised not to operate motor vehicles.

Arterial Aneurysms and Arteriovenous Fistulas: Any patient having an arterial aneurysm, because of the danger of its rupture, should be advised not to operate any motor vehicle. Arteriovenous fistulas may result in heart failure which, if severe, will be a contraindication to the operation of any motor vehicle. Both conditions may be amenable to surgical treatment.

Diseases of the Pericardium: In the acute phase of pericarditis, patients under therapy are unable to operate any motor vehicle. Benign infectious pericarditis of unknown cause does not constitute a contraindication to the operation of a motor vehicle, once the acute phase has subsided.

Chronic Constrictive Pericarditis: Patients having severe cases with venous distention, enlargement of the liver, and peripheral edema should be advised not to operate a commercial or passenger transport vehicle. If the condition is well controlled by therapy, patients with chronic constrictive pericarditis may operate a private motor vehicle safely.

Cerebral Vascular Disease: Patients with inadequate blood flow to the brain because of artherosclerosis of the cerebral vessels are apt to have attacks of syncope or dizziness and should be advised not to operate a motor vehicle. If there have been cerebral hemorrhages, thrombosis, infarctions, transient cerebral vascular spasms, or small areas of cerebral softening with resulting changes in personality, alertness, ability to make decisions, or if there has been actual loss of motor or sensory power, or coordination, such patients should be advised not to operate a motor vehicle. If the resulting changes in function are minimal, with little or no disability, it may be possible for these individuals to drive a private motor vehicle.

Diseases of the Veins: Patients with active thrombophlebitis or a previous thrombophlebitis with resulting edema of the extremities and impairment of use should be advised not to operate a commercial or passenger transport vehicle, and, if sufficient disability exists, they should be advised not to drive a private motor vehicle. Patients with active phlebothrombosis should be advised not to drive a motor vehicle because of the danger of embolization with pulmonary infarction.

Physiological Abnormalities.—Physiological abnormalities and disturbances of functional capacity now will be considered in relation to safe driving.

Cardiac Enlargement: Enlargement of either the right or left ventricle should not in itself be considered a contraindication to the operation of a motor vehicle, but such enlargement does point to the presence of organic heart disease which deserves evaluation.

Diminished Cardiac Reserve: Minor degrees of impairment of function of the myocardium will result in dyspnea on exertion. If this is minimal it should not be a contraindication to the operation of a motor vehicle. If myocardial insufficiency is more marked so that dyspnea prevents the performance of the usual duties involved in the operation of a commercial motor vehicle or is likely to prevent proper performance under emergency conditions, then such patients should be advised not to operate commercial or passenger transport vehicles. If the congestive heart failure is well controlled by therapy, these patients may operate a private motor vehicle. These same considerations apply to either hepatomegaly or peripheral edema resulting from myocardial insufficiency.

Arrhythmias and Conduction Disturbances: Auricular premature beats are of little consequence and do not preclude the operation of motor vehicles. Patients with paroxysmal auricular tachycardia, flutter, or fibrillation with myocardial insufficiency should be advised not to operate a commercial or passenger transport vehicle. If such attacks are well controlled by therapy, then the patients may operate any motor vehicle. Auricular fibrillation of a chronic nature provides the risk of embolization from the auricles, and such patients therefore should not operate commercial or passenger transport vehicles.

Ventricular arrhythmias other than occasional ventricular extrasystoles are usually associated with serious heart disease and frequently are the cause of sudden death. Such patients should be advised not to drive commercial or passenger transport vehicles but may drive private vehicles.

Auriculoventricular block, if of minor degree, is of no significance. Patients with prolonged degrees of atrioventricular block or complete atrioventricular block, if associated with convulsive disorders due to Stokes-Adams syndrome, should be advised not to operate a motor vehicle. If these attacks are controlled by therapy, such patients may operate private motor vehicles.

Pain due to Coronary Arterial Insufficiency: Angina pectoris, coronary insufficiency, and myocardial infarction are all indications of impaired blood supply to the myocardium. Such patients should be advised not to operate commercial or passenger transport vehicles. If angina pectoris is mild and controlled by therapy, then such patients may operate their private motor vehicles. The same is true for patients recovering from a myocardial infarction.

Pain due to Pulmonary Hypertension: The significance of pain due to pulmonary hypertension is primarily in differentiating it from pain due to coronary arterial insufficiency. Patients with pulmonary hypertension are not as prone to sudden death and therefore may, if the degree of pain is not too severe or when well controlled by therapy, operate any type of motor vehicle.

Hypertension: The presence of an elevated blood pressure, due to any cause, above 150-160/90 mm. Hg in itself should not be considered as a contraindication to the operation of a motor vehicle. Complications of hypertension do result in disability contraindicating operation of a motor vehicle. Usually persistent hypertension above 180/100 mm. Hg is accompanied by complications that may be dangerous to driving. Such patients must be examined very carefully to make sure that there has been no involvement of the eyes, brain, heart, or kidney likely to prove disabling for the safe operation of commercial or passenger transport vehicles. When such severe impairment or disability exists, the patient should be advised not to operate private motor vehicles.

Hypotension: Hypotension in itself is not a contraindication to the operation of a motor vehicle. If hypotension results in attacks of syncope, such patients should be advised not to operate a motor vehicle. When these attacks are controlled by therapy, patients may operate a private motor vehicle.

Carotid Sinus Sensitivity: Individuals with carotid sensitivity who experience attacks of syncope should not drive a motor vehicle.

Ophthalmology

Adequate vision is essential for the proper and safe operation of a motor vehicle. Visual potentials can be ascertained by using available vision testing instruments.

Licensing authorities have established visual acuity requirements ranging from 20/30 to 20/70. Two states have no specific visual requirements. Every physician should familiarize himself with the visual requirements of his state's licensing authority.

The patient's perception of what he sees is of great importance. As yet, however, there is no practical way of testing for faulty perception. It is important for drivers to have their vision periodically evaluated, particularly those with significant progressive visual deterioration.

Visual Acuity.—At present we believe that patients whose corrected vision, tested under standard conditions, is 20/40 or better may be advised that this vision is adequate for the task of operating a private vehicle. Those with vision less than 20/40 should be referred to an ophthalmologist to ascertain if vision can be improved. Patients with less than 20/70 corrected vision in the better eye should be advised not to drive.

At present there is no uniformity of opinion regarding the safe driving ability of individuals with visual acuity between 20/40 and 20/70. Furthermore, there are no scientific data available which permit the establishment of fixed standards.

The physician, in serving the best interests of these patients, should consider the conditions under which each patient drives and the vision the patient possesses. He is then in a position to advise the patient whether or not he should drive in congested traffic, in hazardous road conditions, at high speed, or at night. It is hoped that continuing research in this field will lead to a more exact basis upon which to advise patients.

The one-eyed or aphakic driver presents special problems. Many individuals in this category acquire judgment of distance and develop the ability to drive safely. Those individuals who have not acquired this judgment should be advised not to drive and to consult an ophthalmologist.

Regulations for licensing drivers of commercial and passenger transport vehicles usually require higher visual acuity than most licensing agencies require for drivers of private vehicles.

Visual Fields.—Second in importance to visual acuity are visual fields, i. e., form fields. These are obviously important for safe driving, for a driver must of necessity possess some depth and lateral perspective in the horizontal meridian in order to pass approaching vehicles safely as well as being aware of approaching vehicles or pedestrians from the side.

Patients with visual form fields of 140 degrees or more may be advised that this field is sufficient for the task of operating a motor vehicle. Patients with form fields less than 110 degrees should be advised not to drive. The patient with a field between these limits must be evaluated on the basis of the conditions under which he drives and the amount of lateral vision he possesses.

Individuals with markedly constricted fields, such as those suffering from severe glaucoma or retinitis pigmentosa with peripheral blindness, are unfit for safe driving and should be advised not to drive.

Ocular Muscle Imbalance.—The accident potential of ocular muscle imbalance is indirect through causing driver fatigue. However, when diplopia occurs, accidents are directly attributable to the diplopia. Therefore, all patients with uncontrolled diplopia should be advised not to drive a motor vehicle.

Color Blindness.—Color blindness has in the past been considered to be a potential cause of highway accidents. At the present time, however, traffic lights have been standardized, and, except in cases of those engaged in interstate or heavy transport, it is doubtful if color blindness or deficiency is of any great consequence.

Dark Adaptation.—Dark adaptation and susceptibility to glare are of importance in night driving, but at the present time no valid data are available as to their importance in the causation of highway accidents. Of course, dark glasses should not be worn for night driving and windshield tinting should be limited to the upper one-third.

Depth Perception.—Tests for depth perception are inadequate at this time. The road test is still best and is practical.

Otolaryngology

Deafness and dizziness or vertigo due to internal or middle ear disturbances are the principal otological symptoms of significance in the safe operation of a motor vehicle.

Although deafness is a handicap in the safe operation of a motor vehicle, usually it is compensated for quite well. The deaf driver, being fully conscious of his disability, tends to be cautious and fully alert at all times. Moreover, the use of an outside rear view mirror is of great value. The wearing of hearing aids has not proved practical in noisy commercial or passenger transport vehicles. However, in the operation of private vehicles, patients who successfully wear hearing aids frequently find the hearing aid most useful. Thus, much depends on the vehicle, road noise, the patient, and his type of deafness. Although deafness is disqualifying in the operation of a passenger transport vehicle, this is not necessarily so for the operation of a commercial or private vehicle. However, some licensing authorities and the Interstate Commerce Commission have specific regulations in this matter which the physician will need to consult when patients need advice in this area. This information may be secured from the state licensing authority.

Patients subject to attack of Ménière's syndrome or sudden dizziness, no matter what the cause, should be advised not to operate a motor vehicle until proper treatment has controlled such attacks, when he may resume driving a private vehicle but not a commercial or passenger transport vehicle. The character of the attacks may change so there is sufficient warning of the impending attack enabling the patient to drive his vehicle over to the curb or off the highway. In such an event the patient may resume driving a private vehicle.

There are very few laryngological conditions which interfere with the safe operation of a motor vehicle. However, individuals with seriously handicapping speech disorders or any irremedial deformities or diseases of the mouth, nose, and throat interfering with feeding, speech, or breathing should not operate a passenger transport or commercial vehicle. Patients with a tracheotomy should not drive a motor vehicle because of the possibility of sudden obstruction of the tracheotomy.

Surgery and Orthopedics

The role of acute surgical lesions as causes of traffic accidents is slight, for an individual so afflicted is unlikely to be driving. Chronic disabling surgical lesions, in those still able to drive, are apt to be compensated for and are not significant causes of traffic accidents. Of chief concern surgically are the severe injuries sustained by occupants of motor vehicles involved in accidents and how such severe injuries can be reduced through such means as car design, seat belts, and crash helmets. These problems are beyond the scope of this guide.

Many orthopedic handicaps may interfere with safe driving. A guide to aid physicians in evaluating such handicaps is available.[1] It is important to remember that the final acts of driving, however complicated the psychosomatic-mechanical reaction involved, are dependent on the biomechanical efficiency of the bones, joints, and muscles. Moreover, orthopedic aspects overlap other essential abilities for safe driving—for example, the effects of spinal immobility, in limiting the peripheral field of vision, which is so important, particularly at intersections.

The patient must be in such physical condition that he can control a motor vehicle with safety. This means he must have sufficient strength to control the vehicle; turn the steering wheel, and apply the brakes sufficiently to "slide the wheels." He must be able to reach all controls required in the operation of the vehicle, whether by mechanical means on the vehicle or by suitable prosthetic devices. Moreover, those so handicapped must demonstrate that they can successfully operate their vehicles in this manner.

Experience has shown that orthopedically handicapped persons do not as a rule meet with accidents more often than those not so afflicted. It is known that the handicapped person instinctively is more alert to danger and exercises more caution in driving. Ease of muscular fatigue in these individuals needs to be appreciated, but, again, most of these handicapped individuals are accustomed to regulating their energies and avoiding disabling fatigue.

Specific Requirements.—Specific requirements in persons are best considered from the standpoint of body regions as they relate to the static and dynamic demands upon the driver of a motor vehicle. Moreover, shifting of the line of gravity in the seated posture effects efficiency, comfort, and ability of driver performance, particularly in the orthopedically handicapped. All assessments with respect to driver performance must take cognizance of the variance in the center of gravity through the body of the driver and its effects upon the functional capacity of body parts.

Head and Neck Movements.—Relationships and mobility should be normal for operators of commercial and passenger transport vehicles. Variable degrees of restricted movements of the head and neck are compatible with safe operation of private vehicles.

Any limitation of rotation of the head by 50% or more by disease or splinting necessitates compensatory aids to enable these individuals to drive safely. Outside mirrors and swivel type bucket seats can sufficiently aid some of these people. In case of accident, especially when treatment is supplemented by any kind of supportive splinting or bracing, such individuals may be more vulnerable to injury and should be so advised by their physicians. Patients wearing a neck cast or brace should be advised not to drive until recovery has progressed to the point where pain and cervical restrictions of movement are minimal and external support is no longer necessary.

The patient with spastic torticollis should be advised not to drive a motor vehicle. Patients with mild congenital torticollis without pain or significant disability may be advised that it is safe for them to drive.

Thoracic Region of the Spine.—Patients with disabling diseases and deficiencies of the thoracic region of the spine should be advised against driving a commercial or passenger transport vehicle. Many compromises are possible with regard to private vehicles. Patients with arthritis and older injuries if associated with marked deformity or painful restrictions of motion or respiratory excursions should be advised not to drive a motor vehicle. However, proper bucket type swivel seating with restraining seat belt may provide sufficient compensation for some of these individuals. Patients with interscapular pain which causes restriction of motion of the shoulder joint and increases vulnerability to fatigue and irritability should be advised not to drive until they recover.

Mild to moderate degrees of scoliosis do not ordinarily interfere with safe driving. However, patients with severe grades of scoliosis, when it is accompanied by painful arthritis or ease of fatigue, should be advised not to drive a motor vehicle. The scoliotic patient may be helped by seating of the bucket type or other seating specially tailored to his needs, or possibly with the aid of a brace. However, those wearing braces should be carefully evaluated by the physician as to their ability to manipulate a motor vehicle safely. Individuals with extensions under the arms which could interfere with axillary circulation frequently are too incapacitated to drive safely.

Patients with osteoporosis are vulnerable to vertebral fractures from abrupt deceleration and should be so warned. Such patients can be safeguarded by bucket type seating and proper safety restraint, particularly shoulder harnesses and seat belts. With these aids they may be advised that it is safe to drive. Patients with myeloma of ribs and spine should be advised in a similar fashion.

Lumbar Region of the Spine.—The seated position imposes rather unusual stresses and strains on the lumbar region of the spine. These stresses may induce fatigue accompanied by irritability. The seated position calls for a certain amount of compensatory flattening of the normal lordotic curve, which is influenced to some extent by proper mobility in the hip joints. Stiffness of the hip joints puts added strain on the lumbosacral junction and additional flexion forces during abrupt forward decelerations thus making the lumbar vertebrae more vulnerable to compressive fractures. Patients with a stiff hip should be warned of this danger and encouraged to seek seating revisions and shoulder type harness and safety belt restraints for their own safety.

The lumbar region of the spine should be normal for drivers of passenger transport and commercial vehicles. Lumbar abnormality may not incapacitate an individual from safely operating a private vehicle.

Many patients with lumbar deformities, stiffness, and neuromuscular deficits from cord or nerve root defects are not fully competent to operate a motor vehicle under all conditions. Such patients should be advised appropriately to restrict their driving. Although arthritis, osteoporosis, congenital anomalies, and scoliosis commonly are disabling, power steering, power brakes, and semiautomatic transmission are helpful to most of these individuals, enabling them to drive a private vehicle with safety.

Patients with herniated lumbar disks with much pain should be advised against driving, particularly during acute attacks.

Upper Extremities.—Normal functions are required for drivers of passenger transport and commercial vehicles. A one-armed person, provided the one arm is a good one, can operate a private vehicle safely, especially one equipped with power steering and a wheel button. The same is true for the loss of one arm and one leg, which requires the balancing effects of proper protheses.

Hands on the wheel of an automobile, in addition to serving to balance the driver, also are helpful in bracing against rapid deceleration. Obviously, the grasping power of the hands is of basic importance. An adequate number of opposing digits to the thumb are essential for proper gripping. Each individual with impairment of hand function needs to demonstrate sufficient ability to operate properly his private motor vehicle. Power steering is of great assistance to many individuals so handicapped.

Lower Extremities.—Normal function is essential for drivers of passenger transport and commercial vehicles. However, with good arms, even absence of both legs may not prevent the safe driving of a private vehicle with proper protheses and perhaps special hand controls. During prolonged driving, fatigue will accrue from improper buttock and thigh support. Ankylosis of the hip, as it relates to low back disability, has been discussed already.

Deformities of the feet or legs which require special shoes or braces may also require special controls on the vehicle. The foot controls must be spaced far enough apart to avoid pressure on the accelerator when the brake is being sought.

Stability of Joints.—Stability of joints as well as mobility and strength should be evaluated in reaction to driving ability.

Neurological, Emotional, and Psychiatric Disorders

The unhospitalized patient with an emotional, neurological, or psychiatric disorder presents the conscientious physician with a difficult problem. The disability by its very nature may create a special hazard in the safe operation of a motor vehicle. Yet frequently there are strong socioeconomic justifications for the patient continuing to drive.

Inasmuch as several states have in recent years established special procedures for licensing individuals with certain neurologic and psychiatric disorders, physicians should secure copies of these laws and regulations from the state licensing authority and acquaint themselves with the procedures in order properly to advise their patients.

Neurological Disorders.—Convulsive disorders, including major or minor seizures, petit mal, or psychomotor epilepsy are the most frequently encountered neurological disorders impairing driving ability.

Epilepsy: Epileptic patients not receiving medicaments and who have been seizure free for a minimum of two years are considered good risks for the operation of private vehicles but should be advised not to drive a commercial or passenger transport vehicle. Such patients should be advised not to consume alcoholic beverages in any form for at least 24 hours prior to driving. Moreover, fatigue should be avoided and six hours should be the maximum number of hours behind the wheel in one day. Also, epileptic patients should be advised that night driving may be particularly dangerous because the photic stimuli from opposing headlights may precipitate a seizure. Emotional stress should be minimized by avoiding driving in peak traffic hours. These patients should be advised to secure a review of their progress and physical condition at least twice a year by a physician. Epileptic patients under medication should be advised not to drive a motor vehicle until they have been seizure free for a minimum of two years, and then they should drive only private motor vehicles. They should be advised to limit their driving to daytime and avoid rush hours. They represent a risk not only because of the likelihood of a seizure suddenly occurring while driving but, in addition, the medications may produce undesirable side-effects which interfere with driving capabilities.

Faintness, Syncope, and Episodic Weakness: It would be impossible to cover all the syndromes, diseases, or physiological disorders which produce these symptoms. It is important, therefore, that the pattern of these symptoms be evaluated carefully in terms of impairment of driving ability. The isolated occurrence probably is of little concern. Patients having a history of multiple occurrences should be advised not to drive a motor vehicle until a diagnosis can be established and satisfactory corrective measures have been instituted. In instances in which no diagnosis can be made and symptomatic therapy is not effective, the patient should be advised not to drive a motor vehicle.

Narcolepsy: Narcolepsy is rare and infrequently encountered. Its onset is usually during adolescence or adult years and its etiology is poorly understood. The treatment is symptomatic. Patients under treatment should be advised not to drive a motor vehicle until they have been symptom free for two years and are experiencing no adverse side-effects from medicaments. If it becomes desirable to discontinue treatment, such patients should be advised not to drive for two years. If there is no recurrence of symptoms, they may resume unlimited driving.

Disorders Affecting Muscular Control or Coordination: Paralysis agitans, poliomyelitis, hereditary chronic progressive chorea with mental deterioration (Huntington's chorea), multiple sclerosis, hereditary sclerosis, spinal form (Friedreich's ataxia), syringomyelia, muscular dystrophy, cerebral palsy, myasthenia gravis, tumors of the brain and spinal cord, cerebellar degenerative diseases, amyotrophic lateral sclerosis syndrome, post-traumatic syndromes, and intracranial suppurative processes affect muscular control and coordination. The foregoing list of diseases is not complete but suggests the wide variety of processes affecting the nervous system. Each of these will pose special problems with respect to the driving abilities of the individual patient.

The more serious disorders generally cause either rapid deterioration or sufficient functional disability of such degree that the patient will of his own volition cease driving. In those patients with more slowly progressing cases, when the disability reaches a point making driving unsafe, it is the physician's responsibility to recommend to the patient that he discontinue driving.

Mental Deficiency: Patients with an intelligence quotient below 70 and many borderline mentally defectives with an intelligence quotient between 70 and 80 are more susceptible to accidents than normal individuals when faced with emergency situations requiring accurate judgment or decisive action. Patients with intelligence quotients below 70 should be advised not to drive their private vehicles in rush hours, in congested traffic, or under other stress traffic conditions. These individuals also should be advised not to drive commercial or passenger transport vehicles.

Emotional Disturbances.—Many varied stresses and situations create in normal individuals a temporary emotional upset impairing their driving ability. The manifestations occur in three abnormal behavioral patterns. First, the individual is so absorbed in his problem that he is indifferent and inattentive to traffic and the world about him. Second, some individuals become greatly despondent, with actual depression and psychomotor retardation. Such individuals have sufficiently slowed reflexes to make driving a real hazard. Third, many such individuals become antagonistic, impulsive, or openly aggressive with loss of judgment and loss of sense of caution. Patients exhibiting any of these three types of symptoms should be advised not to drive a motor vehicle until they have recovered.

Some patients live under more or less permanent emotional stress. Until, with help and understanding, such patients have worked out an adequate adjustment to the situation, they should be advised not to drive a motor vehicle. Most patients under temporary or persistent emotional stresses producing either aggressive or depressive reactions are unaware of the increased likelihood of an accident. Such patients need to be made fully cognizant of the increased dangers inherent in their situation while being helped to work out a satisfactory solution.

As yet, only limited reliable data are available to aid in identifying drivers most likely to become involved in accidents. The characteristics most clearly related to repeated accidents or high accident rates are very low intelligence, youthfulness, and a personality make-up featured by egocentricity, aggressiveness, antisocial trends, and social irresponsibility.

Psychiatric Disturbances.—The psychoses, affective reactions, schizophrenic reactions, and paranoid reactions in the majority of patients present no recognizable morphologic changes, but the functional disability may be severe. In the majority of instances the frankly psychotic patient will be under hospital care and incapable of driving a motor vehicle. After hospitalization there are in many states special provisions for relicensing these individuals. Physicians should be familiar with these regulations. In exceptional instances where a frankly psychotic patient is being treated on an outpatient basis, the patient and a responsible member of the patient's family should be advised that the patient should not operate a motor vehicle.

Patients who have been returned to the community and require maintenance therapy with the ataractic drugs should be advised not to drive a motor vehicle if drowsiness or syncope occurs. Patients receiving maintenance therapy with the tranquilizers should be observed closely for possible deleterious side-effects from alcohol. Such effects have been reported with certain of the tranquilizer drugs.

Anxiety reactions, dissociation reactions, conversion reactions, phobic reactions, obsessive-compulsive reactions, and depressive reactions are among the conditions observed in the psychoneurotic patient. The patient with a psychoneurosis represents an unknown factor with respect to highway safety. Each case requires separate evaluation regarding alertness, social behavior, and possible psychomotor retardation. If no significant behavioral problem or drug therapy side-reaction exists, then the psychoneurotic patients may be advised that it is safe for them to drive. Careful appraisal, although often difficult, of the driving capacities of all these patients, with sound advice and recommendations to them, provides the physician with an exceptional opportunity for protecting both the safety of his patients and the public. In this manner physicians can make most significant contributions to the prevention of highway accidents.

Alcohol

Alcohol is the responsible factor in a large percentage of the motor vehicle accidents attributed to speed, reckless driving, and driving on the wrong side of the road. Detailed studies in selected areas show that approximately 50% of the fatal accidents involve a drinking driver. If this 50% figure holds nationally, then, in 1958, about 15,000 people died in accidents involving a drinking driver. Although valid data are not available, there is no doubt that many of the accidents which caused injury to about 5,000,000 people in 1958 involved a drinking driver. This situation urgently needs medical consideration.

Pharmacology.—Ethyl alcohol (i. e., grain alcohol, C_2H_5OH) is a central nervous system depressant, even though for years it was called a stimulant. Its effect on human beings is in all phases and stages a depressant. While many individuals will have a sense of exhilaration after consuming alcohol, this is not due to stimulation but to a depression of the inhibitory mechanism. The more recently acquired inhibitions are the first to be affected. Studies reveal that test subjects after consumption of alcohol almost unanimously believe that their performance is unimpaired or even better than usual, whereas objective testing demonstrates that performance is impaired. This, too, is evidence of a depressant action of alcohol—a depression of the critical sense. This depressant action of even small doses of alcohol is of obvious importance in the operation of motor vehicles.

Alcohol and Driving Ability.—Holcomb concluded from his studies that driving performance began to be impaired at a blood alcohol level of 0.05%, or 50 mg. per 100 ml. of blood. Lauer revealed that driving performance in many persons is impaired at an even lower level, 0.035%, and emphasized the importance, at this low level, of such factors as the impairment of judgment, observation, tolerance to glare, and sense of caution, even though muscular performance was not affected.

In 1950 the definitive study by Bjerver and Goldberg appeared and confirmed once again that "the role that alcohol plays in causing traffic accidents is probably considerably greater than appears from official statistics." They ascertained the average threshold of impairment of driving ability in expert drivers, accustomed to consuming moderate amounts of alcohol, as 0.035 to 0.040% alcohol in the blood.

Studies by Smith and Popham of the drivers involved in personal-injury motor vehicle accidents indicate that driving impairment begins at a blood alcohol level of 0.03%. Loomis and West reported in 1959 that "some impairment of ability to perform a simulated driving test could be detected in some individuals when the blood alcohol concentration was as low as 0.03%."

Alcohol Consumption and Blood Alcohol Level.—Almost everyone is interested in the practical aspect of how much liquor of one kind or another can be imbibed before reaching a blood alcohol level considered dangerous for driving. Numerous studies, using individuals accustomed to drinking, all are in full agreement that two 12-oz. bottles of 3.2% beer or 2 oz. of 100 proof whisky consumed within one hour will put the average moderate drinker in the zone of impaired driving ability, i. e., with over 0.035% alcohol in the blood. Three 12-oz. bottles of beer or 3 oz. of whisky will result in more that 0.05% alcohol in the blood of this same individual.

Rate of Oxidation and Elimination.—As the drinker is adding alcohol, the organism is oxidizing it in the liver and eliminating it through the kidneys and the lungs. The concentration of alcohol in the exhaled breath is proportional to the concentration of alcohol in the blood which is circulating through the lungs in a ratio of 2,100:1. The average person of 150 lb. (68 kg.) can oxidize and eliminate about one-third fluid ounce of alcohol per hour, decreasing the concentration of alcohol in his blood by approximately 0.015% per hour. Two hours will reduce the blood alcohol concentration about 0.03% if the individual does not consume more alcohol. This offers a clue to length of the necessary waiting period after drinking before driving.

Measurement of Blood Alcohol Levels.—While direct chemical measurement of the alcohol in the blood is probably the most accurate, the most convenient method is measuring the alcohol in the breath. Several excellent breath testing devices have come into being and are relied upon more and more since the breath alcohol quite accurately reflects the alcohol level of the blood circulating through the lung.

Physician's Advice on Drinking and Driving.—It is not important whether the blood alcohol level is determined on an ascending or descending curve of intoxication; also, the kind of alcoholic beverage consumed, the rapidity of its consumption, or whether it was consumed on a full or fasting stomach is not of material significance. Whether the individual is an experienced drinker with a high degree of tolerance or one who seldom drinks is not the important point. The only significant fact is the amount of alcohol in the individual's blood and the consequent impairment of his driving ability.

The average individual with a blood alcohol level of 0.05% or higher suffers significant deterioration of his driving skill and is a potential menace on the highway. What then, can practicing physicians do to prevent these thousands of deaths and injuries each year? First, patients must learn the basic facts of alcohol consumption and motor vehicle operation. One drink may be tolerated. Two drinks put one in the level of impairment for about two hours. Three drinks are too many.

Summary

The Committee on Medical Aspects of Automobile Injuries and Deaths has compiled in this guide a summary of the pertinent medical data presently available concerning the ability of an individual to operate a motor vehicle safely. Much research remains to be done on factors such as physical disabilities, certain physiological states, and drugs, in connection with safe driving ability. However, on the basis of present knowledge, it is believed that a conscientious medical evaluation of the individual's fitness to drive safely, with appropriate follow-up, can reduce motor vehicle accidents very significantly.

References

1. Guide to Evaluation of Permanent Impairment of Extremities and Back, by Committee on Medical Rating of Physical Impairment, J. A. M. A. (special edition) Feb. 15, 1958.

STATEMENT ON THE DOCTOR-DRAFT ACT

February 2, 1959

Honorable Carl Vinson, Chairman
Committee on Armed Services
U. S. House of Representatives
Washington 25, D. C.

Dear Chairman Vinson:

The purpose of this letter is to submit for the consideration of the Committee on Armed Services the position of the American Medical Association on H. R. 2260, 86th Congress, a bill, which, in part, would extend until July 1, 1963, the induction provisions of the Universal Military Training and Service Act.

With respect to the extension of the special provisions of this Act applicable to medical, dental, or allied specialists, the American Medical Association wishes to reaffirm its position which was outlined in testimony presented in May, 1957, before the House Armed Services Committee on the bill which subsequently was enacted as Public Law 85-62, approved June 27, 1957. At that time, the Association testified that "if the demands for the defense and security of our nation are such that, in the opinion of Congress, it is necessary to have a draft act to maintain the strength of our Armed Forces, then the extension of the present legislation would be one method to insure sufficient physicians for the military services."

The Association also recommended retention of the provisions of the law relating to the national, state, and local committees which advise the Selective Service System in regard to the selection of medical, dental, and allied specialists required by the services. These advisory committees consider, among other factors, the needs of the civilian population in the communities from which these physicians would be taken. The Association is pleased that this provision is a part of the current law.

In regard to specialist categories, the Association recommends, as it did previously in May, 1957, that the word "other" should be substituted for the word "allied" in this section of the law. This would authorize a selective call for other specialists, such as engineers, physicists, other scientists, etc., which might be needed by the military forces. Presently, the law provides only for the selective call-up of medical, dental, or "allied" specialists.

The Association believes that physicians should be registered and classified in the same manner as other citizens in the same age group, deferred for educational purposes in the same manner as other registrants, and called to active duty or inducted under the same general provisions as other registrants deferred for educational purposes.

It is noted that the pending bill proposes a four-year rather than a two-year extension of the Universal Military Training and Service Act. We believe this additional extension of time should be fully explained and justified to the Committee. We believe that this justification is necessary because scientific and technological advances have resulted in rapidly changing concepts of military manpower requirements. Consequently, there has resulted, directly or indirectly, current and projected reductions in the strength of the Armed Forces. It is conceivable that future manpower requirements may be subject to further downward revisions. A lesser period of extension of the law would permit a timely review of military manpower requirements in light of pertinent changes in the then current military situations. The Association believes that this would be particularly desirable with respect to the call-up of medical and allied specialists because of the increasing demands and requirements of the civilian population for the nation's medical and health resources.

As you know from our previous appearances before your Committee, the Association has had a keen and sustained interest in military medicine for many years. Through the Surgeons General of the military services, we have maintained a friendly and close working arrangement in the consideration and advancement of military medical affairs. We feel that the health of the nation requires a careful correlation of military and civilian medicine. In furtherance of this objective, the Association, working with the military services, has attempted to insure improvement in the utilization of medical manpower by the Armed Services and a strengthening of the career incentive program for medical officers.

On behalf of the American Medical Association, I would like to thank you for this opportunity to present our views on H. R. 2260 and to assure your Committee of our willingness to continue our assistance in providing the members of the military services with the finest medical care.

Yours sincerely,
F. J. L. Blasingame, M.D.

STATEMENT ON PROPRIETARY NURSING HOMES

January 26, 1959

Senator John J. Sparkman, Chairman
Subcommittee on Housing
Senate Banking and Currency Committee
Senate Office Building
Washington 25, D. C.

Dear Senator Sparkman:

I am writing this letter to you to express the official views of the American Medical Association with respect to Title II of S. 57, 86th Congress, which I understand, is now pending before your Committee. Our position with respect to this proposal, which would make proprietary nursing homes eligible for mortgage insurance, is one of active support.

Our deep interest in the subject of the health care of the aged and the occurrence of some significant recent developments have prompted me to mention certain activities in this field before outlining the specific reasons for our support of Title II of S. 57.

Since its beginning, more than a century ago, the American Medical Association has been deeply concerned with the medical aspects of caring for the aged. In recent years, however, our interest and activities in this connection have kept pace with the ever-increasing amount of national attention being given to the subject both within the government and among groups and associations outside government. This general trend is understandable, of course, since the proportion of our population over age 65 is increasing at an amazing rate. In 1900 there were only three million of these elderly citizens whereas now there are approximately fifteen million.

For the past several years the American Medical Association has had a Committee on Aging, composed of some of the leading medical authorities in the United States in this field, which has devoted its full effort to this problem. In addition there are forty-five Committees on Aging actively at work in the State medical societies. To facilitate and coordinate the work of these committees, a set of guides for their organization and operation has been developed and made available to them.

As a climax to a series of five regional meetings which were held last year, and in an effort to prepare a positive program for use by the state committees, an A. M. A. National Planning Conference for Medical Society Action in the Field of Aging was held in Chicago on Sept. 13-14, 1958. This Conference was attended by over 175 people including official state medical society representatives from 46 states and the District of Columbia, as well as 27 state health departments. A copy of the official proceedings of this Conference, together with a related brochure entitled "Health Aspects of Aging" are enclosed for the information of the Committee.

In our consideration of the health problems of the aged we have also given serious thought to effective methods of financing medical and hospital care. In considering this facet of the problem, it should be noted that enrollment of older people under voluntary health insurance has increased substantially in recent years. In the last several years alone the percentage of coverage has gone up approximately one hundred per cent. Presently, exclusive of the approximately three million older persons who receive public assistance, more than fifty per cent of those over age 65 have some form of health insurance. Nevertheless, in our opinion, there is a need for further expansion of voluntary health insurance coverage among the aged.

During the last year the Association has conducted or participated in numerous meetings and conferences with commercial insurance carriers and with state and national Blue Cross and Blue Shield Commissions to encourage still greater efforts in the development of new insurance programs and in the expansion of lower cost protection for persons over age 65. These companies, as well as Blue Cross and Blue Shield plans, are now engaged in intensive studies designed to develop new types of policies tailored to meet the needs of the aged ill; present retirement financing of health insurance policies with paid-up status at age 65; use of life insurance after 65 to pay for health care; and the application of deductible and co-insurance to permit coverage of costly illnesses at a low premium rate, among others.

In order to stimulate further the interest of state medical societies and individual physicians in this movement the House of Delegates of the Association approved the following resolution at its Clinical Meeting which was held in Minneapolis in December of 1958:

> For persons over 65 years of age with reduced incomes and very modest resources, it is necessary immediately to develop further the voluntary health insurance or prepayment plans in a way that would be acceptable both to the recipients and the medical profession. The medical profession must continue to assert its leadership and responsibility for assuring adequate medical care for this group of our citizens.
>
> Therefore, the Council on Medical Service recommends to the House of Delegates the adoption of the following proposal:
>
> That the American Medical Association, the constituent and component medical societies, as well as physicians everywhere, expedite the development of an effective voluntary health insurance or prepayment program for the group over 65 with modest resources or low family income; that physicians agree to accept a level of compensation for medical services rendered to this group, which will permit the development of such insurance and prepayment plans at a reduced premium rate.
>
> This recommendation has been studied and restudied by the Board of Trustees and has received its wholehearted endorsement.

In addition to the numerous and varied medical, scientific and socioeconomic activities being pursued in this field, physicians through their associations have, for some time, recognized the need for additional organizational weapons to attack these problems. For many years the American Medical Association was an active participant in the affairs of the Commission on Chronic Illness, in cooperation with representatives of the general public, industry, labor, agriculture, education, religion, social sciences, journalism, health, and welfare. One of a number of studies which were conducted was entitled "Nursing Homes, Their Patients and Their Care." A copy of this study which was published by the United States Public Health Service, is also attached for the information of your Committee.

Last year the American Medical Association joined with the American Hospital Association, the American Dental Association, and the American Nursing Home Association in the formation of The Joint Council to Improve the Health Care of the Aged. In broad outline the program of the Joint Council will include a coordinated plan of research designed to (*a*) determine the extent, utilization, and availability of facilities and the economic status and resources of the aged; (*b*) spearhead the expansion and experimentation in all types of voluntary health insurance coverage for the aged; (*c*) encourage the expansion of health care facilities for the aged; (*d*) encourage the development of community health services for the aged; (*e*) urge state and local legislative bodies to provide realistic financial support for medical, hospital, and nursing home care of aged public assistance recipients; and (*f*) appraise the problems of the aged who are mentally ill and provide an intensification of education, research, and action programs directed toward health problems of the aged at national, state and local levels.

In its work in connection with the over-all medical care problems of the aged, the American Medical Association has long recognized the importance of proper nursing home facilities. For this reason the Association has had a close relationship for some time with the American Nursing Home Association to work toward the development of higher standards for medical care in nursing homes. In February of 1958 the first National Conference on Nursing Homes and Homes for the Aged was held in Washington. Our Association was an active participant at that meeting. On Dec. 16, 1958, a Conference on Nursing Homes and Related Facilities between representatives of our Association, the American Hospital Association, the American Nursing Homes Association, Public Health Service, and Public Assistance Agencies was held in Chicago to discuss current activities and projected programs concerning facilities for the chronically ill and the aged. The purpose of this meeting was to seek a coordinated effort on the part of interested national organizations.

In addition the A. M. A. is currently making a survey of nursing homes throughout the United States. The American Nursing Home Association is also engaged in such a project and is surveying approximately five thousand member homes to obtain data on the cost of care to the patient, the type of patient in the homes and the type of medical care provided.

As an outgrowth of all of these various related activities in connection with the health care of the aged, our Council on Medical Service has prepared a *six-point program the details of which are outlined* in the attached brochure entitled "Medicine's Blueprint for the New Era of Aging."

In conclusion I should like to comment more specifically with respect to the provisions of Title II of S. 57, 86th Congress. As stated at the outset, the American Medical Association has approved and supports a government-insured loan program of the FHA type for non-governmental hospitals and nursing homes whether their ownership is of a nonprofit or proprietary character.

We have taken this position because we believe there is a critical need for new and improved facilities tailored to the specific health requirements of older citizens. It is our understanding that representatives of other organizations such as the American Nursing Home Association have or will appear before your Committee. They have evidence accumulated over recent years showing that they cannot provide service of the desired quality or quantity because they are unable to obtain the credit they need on reasonable terms to permit them to increase the number and size of adequate nursing home facilities.

Under the Hill-Burton program the federal government has for years been assisting public and nonprofit institutions through money grants. It is also our understanding that the Federal Housing Administration is presently offering mortgage insurance for construction of large nonprofit institutional-type homes for the aged which may have a section for those needing nursing care. In our opinion the immediate need is for a similar program of loan guarantees for proprietary organizations, since according to the latest statistics over seventy per cent of nursing home patients are cared for in such facilities.

In the administration of a grant program under the Hill-Burton system and a loan guarantee program under the Federal Housing Administration, we recognize the desirability of cooperation; however, we believe that the loan guarantee program proposed under Title II of the pending bill should be administered by the Federal Housing Administration without mandatory supervision or coordination with the Department of Health, Education, and Welfare.

I would like to request that this letter and attachments, to the extent possible, be made a part of the record of the hearings of your Committee. If you or any of the members of the Committee desire additional copies of the attached material or any further information from our Association, we shall be happy to provide you with anything we have.

Your willingness to permit the American Medical Association to present its views on the pending proposal is sincerely appreciated.

Very truly yours,
F. J. L. Blasingame, M.D.

HEALTH INSURANCE FOR PERSONS OVER 65 YEARS OF AGE

The action of the House of Delegates at its 1958 Clinical Session (Dec. 2-4) adopting a supplementary report of the Council on Medical Service urging the development of special medical care coverage at low premium rates for persons over age 65 brought an immediate response from Donald H. Stubbs, M.D., chairman of the board of directors of Blue Shield Medical Care Plans, the national association of Blue Shield plans.

Dr. Stubbs' announcement stated "Physicians everywhere have been urged to support this proposal and it is especially significant to the 120,000 doctors who are now participating in Blue Shield Plans, because they recognize their civic duty to help provide medical care to their patients under nonprofit programs with local control."

Dr. Stubbs said he believed local Blue Shield plans are ideally equipped to assist the medical profession in developing low cost coverage for senior citizens because each plan is operated under local medical society sponsorship in the area it serves and can put into effect any program to meet the exact specifications of coverage for elder citizens which physicians believe to be desirable. He also pointed out that the plans can be especially helpful in developing low cost coverage under their regular programs to some 2,500,000 subscribers over 65 years of age who have either been enrolled under Blue Shield group programs which ordinarily impose no age limits or who have joined Blue Shield before reaching 65 and have elected to continue their coverage on retirement.

The A. M. A. proposal, according to Dr. Stubbs, calls for a program under which physicians would accept a level of fees related to the modest resources and income of persons over 65 years of age. Such an arrangement, he indicated, would make it possible to provide the coverage at low rates and constitute a program that persons living on retirement incomes could easily afford.

Prepared by the Council on Medical Service.

According to the Blue Shield release, Dr. Stubbs indicated that each of the 64 Blue Shield plans in the United States will be asked to go to work immediately with local medical groups to draft benefit schedules and rates for coverage . . . to meet the needs of persons past 65 years of age. He added that guidance and information would be offered local plans by the national Blue Shield association in Chicago to expedite their efforts in developing their contracts.

To draft suggested patterns of coverages, special committees of the Blue Shield Board were created with the following twofold objectives: 1. To develop a practical pattern of benefits designed to meet the special medical needs of persons over 65 years of age. 2. To suggest a level of medical compensation for those benefits which would permit rates commensurate with the "modest resources or low family income" of persons in this age category.

Certain obvious facts were recognized in approaching these objectives. According to these committees, utilization and cost studies clearly indicated that the incidence of medical care for this age group is greater and, consequently, costlier. But these studies also produced evidence that the problem is not as severe as had been anticipated. It was the conclusion of the committees that the provision of adequate in-hospital medical care benefits must be a part of any program offered to this segment of our population.

Those studies reportedly revealed that, although the incidence of surgery increases in certain categories, other high cost and high incidence procedures, such as tonsillectomies, appendectomies, etc., common in the younger age group, can be minimized. It was the consensus that preexisting conditions will have to be covered after a reasonable (six months) waiting period.

After thorough consideration of these and other factors, the Blue Shield committees recommended that the following benefits be provided with reasonable premium rates to those over 65 years of age with "modest resources or low family income": (*a*) surgery; (*b*) anesthesia; (*c*) in-hospital medical care for 120 days; (*d*) diagnostic x-ray in the hospital, in the hospital outpatient department or doctor's office if hospitalization follows; and (*e*) radiation therapy.

During the course of preparation of the suggested programs, representatives of the Blue Shield staff conferred on two occasions with the Committee on Insurance and Prepayment Plans of the Council on Medical Service seeking its counsel and assistance.

On Jan. 26 the national Blue Shield office submitted the proposal to the local member plans. Subsequently, the Council on Medical Service directed the following memorandum to those constituent associations and component societies sponsoring or approving Blue Shield plans:

> As all of us know, there is a widespread interest in the problems of the so-called senior citizens. This includes problems concerned with health care, as well as the financing of such care. And, since voluntary health insurance is a primary means of financing health care, it is logical that the medical profession should look to insurance or prepayment programs to assist in meeting this new problem.
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> Recognizing this, the House of Delegates, at its Minneopolis Session (December, 1958), adopted a report urging the development of special insurance and prepayment programs for persons over 65 with "modest resources and low family income." A copy of this report and the comments of the Reference Committee are enclosed for your information.
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> As a step in implementing this report, the Committee on Insurance and Prepayment Plans of the Council on Medical Service conferred with representatives of Blue Shield to discuss the types of benefits that might be included in a program for those over 65. As a result, Blue Shield has set forth its suggestions for such coverage in the enclosed Policy Letter to its member plans. The Committee agreed in general with these proposals. It has, however, one important addition which it believes should also be considered. A major effort must be made to provide an alternative to hospitalization. It was agreed by the Committee that every effort should be made to provide for a specified number of office and home calls per year. Such a provision should also permit payment for calls to nursing homes as an alternative to hospitalization.
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> With this addition, and in full recognition that income ceilings and physicians' fees for any program must be viewed in the light of local or state conditions, the Committee recommends that your medical society give earnest consideration to implementing programs set forth by Blue Shield and other groups, which would carry out the intent of the House of Delegates' action.
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> It is the Committee's hope that the medical societies will initiate meetings to discuss this problem. The Committee would also appreciate being informed of any developments that may occur so that the House of Delegates, the Board of Trustees, and the Council on Medical Service may be aware of the progress being made.

The active interest of the private insurance companies is evident from the report of a special meeting of the Health Insurance Association of America held in New York City, Dec. 8, 1958. At that meeting a resolution was approved setting forth principles designed among other things to promote more rapid spread of hospital, medical, and surgical insurance among people aged 65 and over.

Principal features of the resolution are that insurers offering individual coverage (*a*) should continue and accelerate their progress in minimizing the refusal of renewal solely because of deterioration of health after issuance, (*b*) should promptly make available to insurable adults policies which are guaranteed renewable for life, (*c*) should encourage sale of permanent health care insurance where the need for this type of coverage exists, and (*d*) should promptly take steps if they are not presently doing so to offer insurance coverage to persons now over age 65. Insurers writing coverage on a group basis, the resolution added, should (*a*) aggressively promote soundly financed coverages that will continue after retirement and (*b*) encourage the inclusion in group contracts of the right to convert to an individual contract on termination of employment.

MEDICAL NEWS

ALABAMA

Change of Address.—The Medical Association of the State of Alabama announced that subsequent to Feb. 20 all mail for the association should be directed to the following address: The Medical Association of the State of Alabama, 19 S. Jackson St., Montgomery 4, Ala.

Personal.—Richard T. Eastwood, Ph.D., was appointed executive director of university affairs for the University of Alabama Medical Center, Birmingham, effective Oct. 15.——Dr. Durward L. Lovell was appointed director of medical education, Birmingham Baptist Hospitals, Birmingham. He will be responsible for directing the hospitals' intern training program.

ARKANSAS

Dr. Dinning Named Head of Biochemistry Department.—James S. Dinning, Ph.D., associate professor of biochemistry, University of Arkansas Medical Center, Little Rock, was promoted to professor and head of the department of biochemistry to succeed Paul L. Day, Ph.D. Dr. Day resigned recently to become the first scientific director of the United States Food and Drug Administration. Dr. Dinning joined the university faculty in September, 1948, as an assistant professor and left in 1952 to spend one year at the University of Pittsburgh. He is a special consultant to the United States Public Health Service's Metabolism and Nutrition Study Section and this year closed out a five-year term as associate editor of *Nutrition Review*. He is on the editorial board of the *Journal of Nutrition* and is secretary of the Southwest Section of the Society for Experimental Biology and Medicine.

CALIFORNIA

Center for Cardiovascular-Renal Diseases.—A center for intensive treatment of cardiovascular-renal diseases and electrolyte problems was established and is in operation at Saint Joseph Hospital, Burbank. The center is in readiness to receive patients with cardiac or renal failure who may benefit from use of an artificial kidney, "medical" heart-lung machine, or with use of modern physiological monitoring equipment. The center is headed by Dr. Peter F. Salisbury.

University News.—Dr. G. Meyer-Schwickerath, of the University of Bonn, spoke Nov. 14 at the Stanford University School of Medicine on "Treatment of Retinal Lesions and Intra-Ocular Tumors with the Light Coagulator." Dr. Meyer-Schwickerath's lecture was part of a four-day postgraduate conference on ophthalmology at the Medical School devoted to "The Causes of Failure in Intra-Ocular Surgery and Related Problems."

CONNECTICUT

Physiologist Wins International Award.—Dr. John F. Fulton, physiologist at the Yale School of Medicine, New Haven, was named 1958 recipient of the annual George Sarton medal of the History of Science Society, given annually for "outstanding contributions in history of science." Dr. Fulton is a former chairman of the department of physiology at Yale and now holds the rank of Sterling Professor of the History of Medicine. The George Sarton medal was created in honor of Dr. Sarton, Belgian scholar and professor of the history of science at Harvard, who died in 1956. Dr. Sarton founded the History of Science Society in 1912 and its publication, *Isis*, in 1912. The medal was created in 1955 and made possible by the Charles Pfizer Company. Dr. Sarton himself was the first recipient.

Personal.—Dr. David Seligson, formerly associate professor of clinical chemistry in medicine, University of Pennsylvania School of Medicine, Philadelphia, was appointed director of laboratories at Grace-New Haven Community Hospital and associate professor of medicine in the Yale University School of Medicine, New Haven.——The appointment of Dr. Morris A. Wessel, New Haven, to represent the Connecticut State Medical Society on the Governor's Committee on Children and Youth was announced. Dr. Harold M. Clarke, New Britain, was appointed to represent the society at a national conference on the medical care of veterans and their dependents.

FLORIDA

Society News.—The Board of Governors of the Florida Medical Association has announced the appointment of Mr. William Harold Parham as executive director.——The Greater Miami Eye, Ear, Nose and Throat Society, which meets quarterly in March, May, October, and December on Thursday evenings at the McAllister Hotel, Miami, has elected

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

the following officers for 1959: president, Dr. Mariano B. Caballero; vice-president, Dr. Joseph Freeman; secretary-treasurer, Dr. H. Carlton Howard.

HAWAII

Society News.—The following have been elected officers of The Honolulu Pediatric Society for 1959: president, Dr. Duke Cho Choy, Honolulu; recording secretary, Dr. Frances F. Nakamura, 1481 S. King St., Honolulu, Hawaii; corresponding secretary-treasurer, Dr. Calvin C. J. Sia, 1305 Kalakaua Ave., Honolulu, Hawaii.

IDAHO

Society News.—The newly elected officers of the Idaho Academy of General Practice are: president, Dr. Joseph G. Wilson, Moscow; president-elect, Dr. Arch T. Wigle, Pocatello; secretary-treasurer, Dr. Walter W. Wilson, Coeur d' Alene; A. A. G. P. delegates, Drs. Asael Tall, Rigby, and Ralph Buttermore, Grangeville; alternates, Drs. Aldon Tall, Rigby, and Louis F. Lesser, Boise.

ILLINOIS

Clinic for Juvenile Research at Jacksonville.—The State Department of Public Welfare announced Jan. 29 that its tax-supported Institute for Juvenile Research is opening a new regional medical clinic at the Infirmary in the Illinois School for Deaf to provide psychiatric, psychological and psychiatric social services to the emotionally disturbed child and his family for children under 18 years of age residing in Adams, Brown, Cass, Morgan, Pike, Schuyler, and Scott counties. Application forms may be secured from the Springfield regional office or local health departments. Address inquiries to the Institute for Juvenile Research, 404 State Office Bldg., Springfield.

Chicago

Dr. Sulzberger to Give Pusey Lecture.—The William Allen Pusey Lecture of the Chicago Dermatological Society will be given March 18, 7 p. m., at the Illini Union, 715 S. Wood St. Dr. Marion B. Sulzberger, chairman, department of dermatology and syphilology, New York Skin and Cancer Hospital and New York University Postgraduate Medical School and Hospital, will speak on "Some New Aspects on the Biology of the Skin." Preceding the lecture there will be dinner at the Illini Union at 6 p. m. (reservations $4.75 per plate). This is an open meeting and all physicians are invited to the dinner and lecture.

University News.—Dr. J. F. Tait, of the Medical Research Council of Middlesex Hospital Medical School, London, and The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., spoke on "The Secretion and Metabolism of Aldosterone in Normal and Pregnant Subjects" at The Chicago Medical School, Dec. 3.

Name Chairman of Surgery Department.—Dr. John L. Keeley was named professor and chairman of the department of surgery at Loyola University Stritch School of Medicine and head of surgery at Mercy Hospital, succeeding Dr. Harry A. Oberhelman, who will continue on the Mercy hospital staff as a member of the Loyola medical faculty. Dr. Keeley was one of the two American specialists called to Rome in 1958 to attend the late Samuel Cardinal Stritch, archbishop of Chicago. While in Rome he was named a Knight of Gregory of his late Holiness, Pope Pius XII, and Cardinal Stritch conferred the honor upon him. Dr. Keeley was an Arthur Tracy Cabot Fellow in surgery at Harvard in 1936 and 1937, and stayed at Harvard as the *Harvey Cushing Fellow in surgery the following* year. Dr. Oberhelman was chief of surgery at Loyola medical school and Mercy hospital for 17 years.

Hospital Plans Research Expansion.—Ten Chicago business leaders are launching a new board of governors of the Research Institute of Michael Reese Hospital & Medical Center, Mr. Irving B. Harris, president of the center, has announced. Purpose of the new board will be to "plan, program, and finance expansion of medical research." For the first time, Michael Reese reportedly will top one million dollars in research expenditures. About two-thirds of the funds for medical research at Michael Reese comes from governmental agencies, foundations, and such health organizations as the American Heart Association, the American Cancer Society, the American Fund for Psychiatry, the National Nephrosis Foundation, and the Damon Runyon Fund. Michael Reese's Medical Research Institute was founded in 1929, and now numbers 11 full-time departments and three affiliated laboratories.

KANSAS

Regional Physicians Meeting in Wichita.—The American College of Physicians, Kansas Region, will meet March 20 at the Allis Hotel, Wichita. Dr. Fred J. McEwen, of Wichita, is governor of the College for Kansas. Papers which include invited authors are:

Experiences with Cineangiography, Drs. Marvin I. Dunn, Thurl E. Andrews, and E. Grey Dimon, Kansas City.
Clinical Diagnosis of Ventricular Septal Defect, Dr. Alberto Benchimol, Kansas City.
Chronic Nonspecific Pericarditis with Effusion; Case Report, Drs. David Lukens, Calvin R. Openshaw, and Robert C. Tout, Hutchinson.

Milk Alkali Syndrome, Dr. Joseph Meek, Kansas City.
Liver Pathology Following Isoniazid (Marsilid) Toxicity, Dr. Charles G. Hermann, Topeka.

The sessions will close with a dinner (6:15) at which Dr. William C. Menninger, regent of the college, will be guest speaker, presenting "Brains Before Bricks." For information write the American College of Physicians, 4200 Pine St., Philadelphia 4.

MASSACHUSETTS

Appoint Acting Department Heads.—The appointments of Eric G. Ball, Ph.D., as acting head of the department of biological chemistry and of Dr. Maurice M. Tolman as acting head of the department of dermatology were announced by Dr. George P. Berry, dean of the faculty of medicine, Harvard University, Boston. Dr. Ball, who has served as a member of the faculty of medicine at Harvard since 1940, succeeds Dr. A. Baird Hastings, who has retired and has become a member of the resident research staff at the Scripps Clinic and Research Foundation, La Jolla, Calif. Dr. Ball is professor of biological chemistry at Harvard and chairman of the division of Medical Sciences. Dr. Tolman, assistant clinical professor of dermatology at Harvard, where he has taught since 1940, succeeds Dr. Chester N. Frazier, who retired in 1958. Dr. Tolman is acting chief of the dermatology service at the Massachusetts General Hospital.

MICHIGAN

Personal.—Dr. Starling D. Steiner has been appointed medical director of General Motors, effective December 1. He succeeds Dr. Max R. Burnell, who retired on Nov. 1. Dr. Steiner, who has been medical director of the Oldsmobile Division of General Motors in Lansing since 1946, is currently serving as treasurer of the Ingham County Medical Society.——Dr. William A. Fellner has been appointed medical director of General Motors central office, Detroit, effective Feb. 1. He replaces Dr. William J. Fulton, who is retiring.

Annual Conference on Nutrition.—The fifth annual Nutrition Conference, sponsored by Wayne State University College of Medicine, will be held on Friday, March 20. Speakers on the general subject "Inorganic Factors in Nutrition" will include George K. Davis, Ph.D., of the University of Florida; Dr. William B. Schwartz, of Tufts Medical School; Dr. Carl V. Moore, of Washington University; and David M. Hegsted, Ph.D., of Harvard University. Members of the American Medical Association are cordially invited. For information write Mr. James M. Orten, Chairman, Publicity Committee, Wayne State University, 1401 Rivard St., Detroit 7.

Society News.—The Michigan Academy of General Practice congress of delegates convened Nov. 11 and the following officers were elected: Dr. Clark W. Royer, Battle Creek, installed as president by Dr. Francis P. Rhoades, Detroit, retiring president; Dr. Howard C. Rees, Grosse Pointe, president-elect; Dr. Earl C. Long, Detroit, secretary; Dr. Lyle W. Korum, Detroit, treasurer; Dr. C. Howard Ross, Ann Arbor, speaker; Dr. Aaron C. Stander, Saginaw, vice-speaker.

MISSISSIPPI

Society News.—The Mississippi Academy of General Practice concluded its 10th annual meeting recently with Dr. A. T. Tatum, Petal, raised to presidency. Newly elected officers are Drs. R. J. Moorehead, Yazoo City, president-elect; Louis F. Rittelmeyer, Jackson, vice-president; and J. R Bane, Jackson, secretary-treasurer.

MISSOURI

Dr. Mason to Give Annual Lecture.—Dr. Michael L. Mason, professor of surgery, Northwestern University School of Medicine, will present the 10th annual Dr. F. G. Thompson Sr. Lecture on Thursday evening, May 21, at the Thompson, Brumm, Knepper Clinic and Hospital, in St. Joseph. The title of the lecture will be "Treatment of Acute Injuries to the Hand."

NEW JERSEY

Annual Heart Seminar.—The New Jersey Heart Association will hold its annual scientific seminar in the Essex House Hotel, 1050 Broad St., Newark, April 1, at 2 p. m. The program is as follows:

Surgical Approach to Coronary Artery Disease, Dr. Claude S. Beck, Cleveland.
Current Views on the Causation of Atherosclerosis, Dr. Russell L. Holman, New Orleans.
Controversial Views in the Management of the Atherosclerotic Patient, Dr. Samuel A. Levine, Boston.
The Recognition of the Atypical Coronary Occlusion, Dr. William Likoff, Philadelphia.

Dr. Norman Reitman is president of the New Jersey Heart Association, and Mr. Howard W. Dayton, 60 Park Place, Newark 2, N. J., is executive director.

NEW YORK

Welsh Guest.—Dr. Arthur G. Watkins, Dean of Clinical and Postgraduate Studies at the Welsh National School of Medicine, Cardiff, England, was the guest of the pediatrics department at Albany Medical College Feb. 16 and 17. Dr. Watkins, who is also professor of child health at the Welsh School and pediatrician at the United Cardiff Hospitals, served as professor pro tem of pediatrics during his stay. He addressed junior medical students on Monday, and spoke before the entire student body and faculty on Tuesday.

Open Applications for Medical Supervisor.—The New York State Department of Civil Service will accept applications until April 10 from qualified candidates for the position of supervisor of school medical services, State Education Department. No written or oral test will be required. Candidates will be rated on their training and experience in relation to the duties and requirements of the position. At present there is one vacancy in Albany and another is anticipated. Candidates must possess a license issued by New York State to practice medicine or be eligible to enter the examination for such a license and must have two years of satisfactory experience in the practice of medicine, of which one year must have included service as a school physician. The annual salary range for this position, which is open only to legal residents of New York State, is $8,750 to $10,520. A supervisor of school medical services performs field and office work in the supervision and guidance of the health services program in the schools of the state. For applications write to Recruitment Unit, New York State Department of Civil Service, State Campus, Albany 1, N. Y.

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New York City

Dr. Brunsting to Give Memorial Lecture.—The department of dermatology and syphilology of New York University Post-Graduate Medical School announced that the second Howard Fox Memorial Lecture will be given by Dr. Louis A. Brunsting Sr., April 21, 8 p. m., in the auditorium of Alumni Hall, 550 First Ave., New York City. The title of his talk will be "Porphyria Cutanea Tarda."

Dr. Wangensteen to Lecture.—The annual Walter L. Niles Memorial Lecture, sponsored by Nu Sigma Nu, Tau Chapter, will be given by Dr. Owen H. Wangensteen, chief of surgery, University of Minnesota, Minneapolis, at 8 p. m., March 18, in the auditorium of the Cornell University Medical College, 1300 York Ave., on "Studies in Peptic Ulcer." A dinner in honor of Dr. Wangensteen will be held before the lecture. The lecture is open to medical students and members of the profession.

Hospital News.—The celebration of the 100th anniversary of the third (NYU) surgical division of Bellevue Hospital Center was a highlight of the New York University College of Medicine Alumni Day ceremonies Feb. 21. Dr. Frank B. Berry, assistant secretary of defense (health and medical) and former director of Bellevue's first surgical division, received the University Bronze Medal and gave the principal address of the day. Additional awards presented were the association's annual distinguished service award to Dr. John H. Mulholland, chairman, department of surgery, and the presidential citation to Dr. Henry M. Scheer, former president of the association.

Memorial Fellowship for Cancer Research.—The New York Cancer Research Institute awarded the first Oliver E. Spencer Memorial Fellowship to New York University College of Medicine. The fellowship, established by friends and relatives of the late Oliver E. Spencer, who died of cancer at the age of 25, will provide a one-year training and research scholarship to a physician specializing in cancer and selected by Dr. Donal Sheehan, dean. The first incumbent is Dr. Erlinda Tobillo Novales, of Manila, The Philippines. Upon receiving her M.D. degree in 1955 from Santa Tomas University, she came to the United States for her residency training at New York City's Gouverneur Hospital and the New York Infirmary, where she is now chief resident in medicine.

Neurological Institute Celebrates Anniversary.—The year 1959 marks the 50th anniversary of the founding of The Neurological Institute of New York, specifically set up as a specialty hospital for the medical and surgical treatment of the nervous system. The institute in 1929 became affiliated with the Presbyterian Hospital of New York as a part of the Columbia-Presbyterian Medical Center. To commemorate the institute's 50th anniversary, a series of special events have been planned by Columbia University and the Presbyterian Hospital, and by various societies in neurology and neurosurgery. On March 10 a joint meeting of the New York Neurological Society and the Section of Neurology and Psychiatry of the Academy of Medicine was held. On April 27-28 the Society of Neurological Surgeons will hold its 50th meeting at the institute. A special anniversary celebration will be held at the Columbia-Presbyterian Medical Center May 15-16. Scientific sessions at which alumni and guests will speak will be held and there will be a commemorative dinner at the Waldorf-Astoria Hotel.

On May 16 a special convocation of Columbia University and the Presbyterian Hospital will be held at the Medical Center.

PENNSYLVANIA

Philadelphia

Personal.—Dr. I. S. Ravdin, vice-president for medical development, University of Pennsylvania, and Dr. John McK. Mitchell, vice-provost of the university and dean of the School of Medicine, were appointed to the Surgeon General's Consultant Group on Medical Education, Dr. Leroy Burney, surgeon general of the U. S. Public Health Service has announced.——Dr. Orville C. King was named director of the division of surgery for Pennsylvania Hospital department for sick and injured, Eighth and Spruce Streets. This announcement coincides with Dr. King's appointment as professor of clinical surgery, University of Pennsylvania School of Medicine.

RHODE ISLAND

Dr. Dailey Appointed State Health Director.—Governor Christopher Del Sesto of Rhode Island announced the appointment of Dr. Jeremiah A. Dailey, of Edgewood, as director, Department of Health, State of Rhode Island. Dr. Dailey retired from the United States Army at Fort George G. Meade, Md., Jan. 31. At the time of his retirement he was commanding officer, 68th Medical Group.

Hospital News.—Dr. Henry N. Harkins, professor of surgery and executive officer, department of surgery, University of Washington School of Medicine, Seattle, and surgeon-in-chief, King County Hospital (Seattle), will serve as surgeon-in-chief pro tempore at the Rhode Island Hospital, Providence, on March 19-21.

TENNESSEE

University News.—Dr. James S. Speed, head of the department of orthopedic surgery, University of Tennessee College of Medicine, Memphis, since 1941, has resigned his administrative duties but will continue as professor in the department. Dr. Speed's position as head of the department will be taken by Dr. Harold B. Boyd, who was advanced from associate professor to professor.

TEXAS

Dr. Wallace Wins Caldwell Award.—Dr. Stuart A. Wallace, chairman, department of pathology, was presented with the George T. Caldwell award, naming him "Pathologist of the Year for the State of Texas" at a meeting of the State Clinical Pathologists in Houston. The presentation was made at a banquet Jan. 24 "in recognition of long and distinguished service to mankind in the field of Pathology in Texas." Dr. Wallace has been associated with Baylor College since it was located in Dallas and became chairman of the department when the Houston move was made. The award, in memory of the late Dr. George T. Caldwell, who was professor of pathology at Baylor College of Medicine in Dallas, was established by Mrs. Caldwell and family about five years ago.

VIRGINIA

Meeting of Physicians in Hot Springs.—The American College of Physicians, Virginia Region, will meet March 21 at the Homestead, Hot Springs. Thirteen papers are scheduled for presentation, including the following which have invited guest authors:

Evaluation and Management of Electrolyte Problems in Heart Failure, Drs. Julian R. Beckwith Sr., Nuzhet O. Atuk, and J. Edwin Wood Jr., Charlottesville.

Pathogenesis of the Anemia in Myxedema, Drs. Jason E. McClellan and Byrd S. Leavell, Charlottesville.

Long-Term Anticoagulant Therapy, Drs. Frank E. Taylor, Charles L. Crockett Jr., and R. Earle Glendy, Roanoke.

The Coagulation Deficiencies with Report of a Case of Christmas Disease, Dr. Harry I. Johnson, Roanoke.

The Co-Existence of Pheochromocytoma and Unilateral Adrenocortical Hyperplasia, Drs. Gerald A. Williams, Charlottesville, William W. S. Butler, III, Roanoke, and Kenneth R. Crispell, New York City.

Clinical Usefulness of a Potent New Oral Diuretic, Drs. Gordon F. Cavell, Eugene M. Wyso, and David W. Richardson, Richmond.

Cardiotoxic Effects of Quinidine and Its Treatment with Molar Sodium Lactate, Dr. Dewey J. Bailey, Charlottesville.

A business meeting will precede a meeting with the Virginia Society of Internal Medicine at 4 p. m. Guest speaker will be Dr. Dwight L. Wilbur, San Francisco, president of the college. Dr. Charles M. Caravati is governor of the college for Virginia.

WEST VIRGINIA

Surgeons Meeting in White Sulphur Springs.—The annual meeting of the West Virginia Chapter of the American College of Surgeons will be held at The Greenbrier in White Sulphur Springs, April 3-4. Dr. Cornelius E. Sedgwick, of the Lahey Clinic, will present papers on "Portal Hypertension," "Tumor of the Neck," and "Surgical Treatment of

Thyroid Disease." Dr. David M. Hume, chairman, department of surgery, Medical College of Virginia, Richmond, will speak on a surgical subject of general interest. A cordial invitation has been extended by the West Virginia Chapter to all practicing physicians in the state. Information may be obtained by writing Dr. Victor S. Skaff, Secretary, West Virginia Chapter, ACS, 807 Atlas Building, Charleston 1, W. Va.

Appoint Acting Director of Mental Health.—Dr. Margaret T. Ross, director of community service, West Virginia State Department of Mental Health, was named by Governor Cecil H. Underwood as acting state director of mental health. She succeeds Dr. William B. Rossman of Charleston, who resigned. Dr. Richard J. Lilly, of Weston, superintendent of Weston State Hospital, had been appointed as successor to Dr. Rossman, and he came to Charleston and took the oath of office. However, late in January the question of Dr. Lilly's eligibility for the office was raised, inasmuch as he has not been a citizen of West Virginia for one year, as required by state law. On Feb. 4, the appointment of Dr. Lilly was withdrawn temporarily by Governor Underwood, who at that time indicated that he will reappoint him to the office next May, when he will have been a resident of the state for a year.

WISCONSIN

Dr. Morton Wins Award.—Newton E. Morton, Ph.D., assistant professor of medical genetics in the University of Wisconsin Medical School, Madison, was named to receive the Lederle Medical Faculty award of $18,000, given by the Lederle Laboratories and designed "to provide support for continued development of a promising teacher and investigator in fields of medicine and human biology." Dr. Morton, who serves as an associate editor of the *American Journal of Human Genetics*, will be supported under the grant for three years.

GENERAL

Booklet on Manuscript Preparation.—To facilitate the work of authors and editors of their journals, S. Karger, Inc., recently issued a booklet containing some rules for the preparation of manuscripts and bibliographies with a list of abbreviations of titles of current medical periodicals. The abbreviations of titles of periodicals have been taken with some minor deviations, from the list of World Medical Periodicals compiled by the World Medical Association based on the World List of Scientific Periodicals prepared under the auspices of UNESCO. The booklet has also been issued in German and French. For information write S. Karger, Inc., Swiss Bank Corporation, New York City.

Citizens' Committee on Health.—*Formation of an* ad hoc citizens' committee to increase public understanding of the principles underlying increased United States support of international health work was announced Feb. 12 by Dr. Howard A. Rusk in an address before a Brotherhood Week Luncheon of the National Conference of Christians and Jews in New York City. General Omar Bradley is chairman of the new group, known as the Committee on Health for Peace, and Detlev W. Bronk, LL.D., president, Rockefeller Institute for Medical Research, is chairman of its Scientific Advisory Committee. The Committee on Health for Peace will not engage in fund-raising activities; nor will it attempt to duplicate the work of the National Citizens Committee for the World Health Organization. Its function will be solely to increase public understanding of the importance of international cooperation in health and medical research. The activities would be entirely educational and would be initially centered on the International Health and Medical Research Act of 1959 which has been introduced in the Senate by Senator Lister Hill, Alabama, with 58 senators as co-sponsors, and in the House of Representatives by Representative John Fogarty, Rhode Island.

Invite Nominations for Research Award.—Nominations for the eighth Kimble Methodology Research Award are being accepted until June 1, 1959. This award, which gives recognition to the application of scientific knowledge to the Public Health Laboratory, was established by the Kimble Glass Company of Toledo, Ohio (subsidiary of the Owens-Illinois Glass Company), and is sponsored by the Conference of State and Provincial Public Health Laboratory Directors. The award of $1,000 and silver plaque will be presented at the annual meeting of the conference to be held in Atlantic City, N. J., in October. Rules governing nominations include:

(1) The candidate's work should be *either:*
  a. A fundamental contribution which serves as a baseline for development of diagnostic methods which fall within the province of the public health laboratory.
  b. The adaptation of a fundamental contribution to make it of use in a diagnostic laboratory.
(2) Candidates should be from the United States, its territories, or Canada.
(3) Nominations must be covered by six reprints with six summaries and bibliography or, if reprints are not avail-

able, by six summaries with bibliography. A statement which justifies the recommendations of the study must be included.

(4) Nominations may be made by the authors, associates, or by others. Documentary evidence, etc., should not be signed by the nominator. The nomination, however, should be accompanied by a letter of transmittal.

(5) Nominations received after June 1 will be considered for nomination in 1960.

(6) Nominations of a piece of work where there is more than one author is permissible. (If such work is selected, division of the cash award shall be arranged between the workers themselves.)

(7) The materials submitted to the Nominating Committee will not be returned to the sender.

Send nominations to E. T. Bynoe, Ph.D., Chairman, Nominating Committee, Kimble Award, Laboratory of Hygiene, Department of National Health and Welfare, Ottawa, Ontario, Canada.

CANADA

Prize for Paper on Fertility.—The Canadian Society for the Study of Fertility announced the award of the 1958 "Ortho" prize to Dr. Charles P. Leblond and Assistant Professor Y. Clermont, of the department of anatomy, McGill University, for their paper on "Differentiation and Renewal of Spermatagonia in the Monkey Macacus Rhesus." The "Ortho" prize was $1,000 for 1958, as the prize of $500 for 1957 was not awarded and had accumulated. Those interested in submitting a paper to the society for the 1959 "Ortho" prize of $500 must do so before June 1. Details may be obtained through Dr. Jean F. Campbell, Secretary-Treasurer, The Canadian Society for the Study of Fertility, 238 Queen's Ave., London, Ontario.

FOREIGN

Pediatric Convention in Italy.—Under the auspices of the Italian Society for Pediatrics (Societa Italiana di Pediatria) an International Pediatric Convention of the Latin Nations, will be held in San Remo, Italy, Sept. 24-27. The convention will be under the chairmanship of Prof. Giovanni De Toni, director of the pediatric clinic "Gaslini" of the University of Genova. The topics for discussion will be the following:

(1) Regional Pathology—the speakers chosen will report on the infantile pathology predominant in their respective regions, and on its changes during the last 20 years.

(2) Disease of Metabolism—the speakers will report on the specific topic of research.

(3) The Growth of the Child, Normal and Pathological Conditions.

Papers on the three topics will be accepted. For any information write to the Secretaries of the Convention (Dott. Prof. Ettore De Toni e Dott. Prof. Piero Salomone) c/o Pediatric Clinic "Gaslini," Genova-Quarto, or to the President of the Executive Committee: Dott. Prof. Giuseppe Cotellessa c/o Azienda Autonoma di Soggiorno e Turismo, Palazzo Riviera, San Remo (Italy).

Congress of Red Cross in Spain.—Dr. Carlos Blanco Soler, president of the first National Medical Congress of the Red Cross of Spain, has announced that the congress will be held in Madrid, May 20-23, under the auspices of the Higher Assembly of the Red Cross. Official topics are as follows:

Radioactivity.
Congenital Heart Diseases: Clinical, Diagnosis and Treatment of Interauricular Defects.
Rehabilitation and Recuperation of Invalids.
Blood Transfusion.

There will be a symposium on medicine and surgery of emergency, with Dr. Soler presiding. For information and registration write the Secretaria General Asamble Suprema, Paseo de Eduardo Dato, 16, Madrid, Spain.

Congress of Health Workers in Paris.—The sixth International Health Workers' Congress and Equipment Exhibition will be held in Paris, at the Parc des Expositions (Porte de Versailles), June 9-12 under the auspices of the journal "Techniques Hospitalieres Medico-Sociales et Sanitaires." It will be organized under the patronage of the French Minister of Public Health and the Population. The central theme will be "The Patient in the Hospital of the Future—The Functions of the Health Team." The chairman of the congress is Dr. Le Gorgeu, member of the Council of State and chairman of the National Committee for Hospital Organization. Hospital workers from all countries are cordially invited to participate. A hospital exhibition will include models of operating suites, wards, laboratories and technical equipment. Information on the program, exhibition space, hotel accommodation, etc., may be obtained from the Secretary-General, 37 rue de Montholon, Paris 9e.

DEATHS IN OTHER COUNTRIES

Dr. Gerin–Lajoie Dies.—The president-elect of the World Medical Association, Dr. Leon Gerin–Lajoie, Canadian gynecologist, died Feb. 14. He was president of the International Federation of Obstetricians and Gynecologists and vice-dean of the faculty of medicine at the University of Montreal. Dr.

Gerin-Lajoie was a founder of the Quebec division of the Canadian Medical Association and had served as its president.

CORRECTION

Report on 1958 Mortality.—In an item appearing in the Feb. 14 issue of The Journal, Medical News section, under this side head, the figures 916 per 1,000 and 912 should have read 9.6 and 9.2, respectively.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. Applications now on file. *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Washington, D. C., Denver, Colorado and Rochester, Minn., Mar. 26-27. Deadline for filing application was Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application was Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Public Health.* Minneapolis, Boston, Baltimore, Chapel Hill, North Carolina and New Orleans, April 9-11; Berkeley, Calif., April 23-25; Pittsburgh, April 16-18. *Occupational Medicine.* Chicago, April 24-26. *Aviation Medicine.* Los Angeles, April 24-26. Final date for filing all applications is March 16. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application was Nov. 1. *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Oral.* Los Angeles, September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

NAVY

Tissue Bank Training Course.—A two-week Tissue Bank Training Course offered at the National Naval Medical Center, Bethesda, Md. is now available to any eligible inactive naval reserve medical officer. This training may commence on any Monday morning and provides orientation in the operation and administration of a tissue bank. It includes (1) indoctrination in the methods of tissue procurement; (2) storage and dispensing; (3) tissue culture; (4) tissue chemistry; (5) processing excised tissue and allied short and long-term research projects in the tissue culture and tissue chemistry fields; (6) indoctrination in the medicolegal aspects of homotransplantation; (7) the procedure for obtaining permission for tissue donations; and (8) familiarization with the operation of the Tissue Bank Registry and all other administrative practices associated with tissue banking.

Reserve medical officers from the First, Third, Fourth, Fifth, Sixth, Eighth, and Ninth Naval Districts may attend this course on a limited quota basis authorized by the chief of naval personnel. Security clearance is not required.

Surgeon General Reappointed.—Rear Adm. Bartholomew W. Hogan was reappointed as surgeon general of the Navy for a period of two years, or until Feb. 15, 1961. He entered the service on June 6, 1925. In the early months of World War II, he served on the USS Wasp and was aboard that carrier when she was torpedoed in the South Pacific on Sept. 15, 1942. For heroic service during this action, he was awarded the Silver Star medal.

Personal.—Capt. A. J. Cerny has assumed command of the U. S. Naval Hospital, Guantanamo Bay, Cuba, relieving Capt. L. A. Newton, who retired on Jan. 31. Other medical officers retired were Captains F. V. Berley, M. J. Hantover (temporary disability), G. A. Gray, and H. L. Weaver.

VETERANS ADMINISTRATION

Treatment Centers for Mental Illness.—The first mental hygiene day center for treatment of veterans with service-connected mental illness was established at the VA outpatient clinic in Brooklyn, N. Y. More such clinics will be established within the next few years. The day center program is designed primarily to provide more and better outpatient treatment for the increasing number of veterans being released from VA hospitals after treatment for service-connected schizophrenia. Many of these patients need a great deal of help through the VA outpatient treatment program if they are to adjust to community living and avoid rehospitalization. The clinic director, Dr. Philip R. Casesa, said about 75 patients will spend the major part of their time at the new day center in a therapy and planned living program under the supervision of psychiatrists, psychologists, and social workers. In addition to individual and group psychotherapy and educational and occupational therapy, this program will include social and recreational activities carried out with the assistance of volunteers from the community. New tranquilizing drugs and improved treatment programs are increasing the number of patients, especially schizophrenics, being released from VA mental hospitals.

PUBLIC HEALTH SERVICE

Health Statistics.—A new report entitled "Hospitalization—Patients Discharged from Short-Stay Hospitals, July 1957-June 1958" has been published by the Public Health Service. For this report, the surveyed population consisted of the civilian noninstitutional population of the country. The data refer to persons in this population group who were discharged from the hospitals during the year. The short-stay hospitals include general, maternity, and other types in which most patients stay for less than 30 days. The number of patients discharged from such hospitals averaged 99.4 per 1,000 of the surveyed population. Among the group discharged, the average length of stay was 8.6 days. Next to childbirth, the most frequent cause of hospitalization was the respiratory diseases, including tonsil and adenoid conditions. The report is Public Health Service Publication no. 584-B7 and may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 30 cents per copy.

Clinical Center Pamphlet Series.—The Clinical Center at the National Institutes of Health is publishing a series of pamphlets describing the methods and procedures used at the center. The first, "A Manual for Metabolic Balance Studies" by Marie M. Ceglarek, R.N., Bertha E. Bryant, R.N., and G. Donald Whedon, M.D. (PHS publication no. 607), is now available at 20 cents a copy from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C.

Personal.—Dr. William B. Sherman, associate attending physician of Presbyterian Hospital and attending physician at Roosevelt Hospital, New York City, and Dr. William W. Frye, professor of tropical medicine and dean of the school of medicine, Louisiana State University, New Orleans, have been appointed to the National Advisory Allergy and Infectious Diseases Council. They will advise and make recommendations to the surgeon general regarding research grants.

DEATHS

Anderson, Donald Carl Ⓜ West Palm Beach, Fla.; University of Minnesota Medical School, Minneapolis, 1945; interned at the Naval Hospital in San Diego, Calif.; veteran of World War II and Korean War; died Dec. 8, aged 41.

Ard, Robert Wilson Ⓜ Hagerstown, Md.; Syracuse University College of Medicine, 1948; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; resigned from the regular Navy on March 6, 1953; served in the U. S. Public Health Service Reserve; veteran of World War II and Korean War; died Dec. 20, aged 34.

Arneberg, John Gyro, Grand Forks, N. D.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1905; associated with Grand Forks Deaconess Hospital and St. Michael's Hospital; died Dec. 17, aged 83.

Audet, Louis Eugene Ⓜ Williamsport, Pa.; Tufts College Medical School, Boston, 1930; died in the Divine Providence Hospital Dec. 19, aged 54.

Bachman, David Floyd Ⓜ Bethlehem, Pa.; Medico-Chirurgical College of Philadelphia, 1912; formerly county coroner; died in St. Luke's Hospital Dec. 22, aged 74.

Barrow, John Vincent Ⓜ Los Angeles; Rush Medical College, Chicago, 1911; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served on the faculties of the College of Medical Evangelists in Loma Linda and Los Angeles and the Medical Department of the University of Southern California; past-president and vice-president of the Los Angeles County Medical Association, of which he was a councilor; served on the staffs of the California, Los Angeles County, and St. Vincent's hospitals, and the Hospital of the Good Samaritan; died Dec. 17, aged 81.

Batory, Roman Julius Ⓜ Stroudsburg, Pa.; Hahnemann Medical College of Philadelphia, 1930; interned at Women's Homeopathic Hospital in Philadelphia, where he served a residency; served a residency at Hamburg State Sanatorium for Tuberculosis in Hamburg; veteran of World War II; member of the American College of Chest Physicians; on the staff of the General Hospital of Monroe County in East Stroudsburg; died Dec. 21, aged 55.

Blumenschein, John Charles Ⓜ Independence, Mo.; Washington University School of Medicine, St. Louis, 1943; interned at Virginia Mason Hospital in Seattle; served a residency at St. Joseph Infirmary in Atlanta, Ga.; associated with the Independence Sanitarium and Hospital; died in Mogate, Honduras, Central America, Dec. 14, aged 40.

Blydenburgh, George Dean, Byesville, Ohio; University of Cincinnati College of Medicine, 1946; interned at White Cross Hospital in Columbus, Ohio; formerly an officer in the medical corps, Army of the United States; died in Columbus Dec. 28, aged 37.

Booth, George Randolph Ⓜ Wilburton, Okla.; Memphis (Tenn.) Hospital Medical College, 1904; died in the McAlester (Okla.) Hospital Dec. 14, aged 74.

Bowles, James Puryear Ⓜ Captain, U. S. Navy, retired, Richmond, Va.; Medical College of Virginia, Richmond, 1911; entered the U. S. Navy Jan. 24, 1921, and retired March 1, 1947; died in the U. S. Naval Hospital Philadelphia, Dec. 24, aged 73.

Breckwedel, Harry Benjamin, Newport Beach, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1900; died Dec. 18, aged 85.

Cannon, Vern Edward, Decatur, Ill.; Chicago College of Medicine and Surgery, 1914; veteran of World War I; on the staff of St. Mary's Hospital; died Jan. 6, aged 68.

Catto, William Bruce Ⓜ El Reno, Okla.; University of Louisville (Ky.) Medical Department, 1908; on the staff of the Park View Hospital; died in Oklahoma City Dec. 7, aged 75.

Cloutier, Doria Marie, Albuquerque, N. M.; University of Wisconsin Medical School, Madison, 1950; died in the Bernalillo County–Indian Hospital Dec. 17, aged 36.

Cochran, J. Lawrence Ⓜ Carroll, Iowa; University of Tennessee College of Medicine, Memphis, 1931; veteran of World War II; president of the Carroll County Medical Society; county coroner; secretary-treasurer of the Iowa Coroners Association; member of the Aero Medical Association; associated with St. Anthony's Hospital, where he died Dec. 24, aged 50.

Coulter, William James, Toledo, Ohio; Toledo Medical College, 1900; served as a member of the staff of the Toledo Hospital; died Dec. 10, aged 91.

Ⓜ Indicates Member of the American Medical Association.

Crounse, Kenneth Eugene Ⓜ Albany, N. Y.; Albany Medical College, 1924; veteran of World War I; formerly on the faculty of his alma mater; consultant, Moses-Ludington Hospital in Ticonderoga; died in Delray Beach, Fla., Dec. 26, aged 61.

Darrin, Charles Bennett, Seattle; Bellevue Hospital Medical College, New York City, 1887; died in the King County Hospital, Harborview Dec. 3, aged 94.

Decker, Elmer Raymond Ⓜ Sunbury, Pa.; Medico-Chirurgical College of Philadelphia, 1910; veteran of World War I; consultant at Federal Penitentiary at Lewisburg; on the staff of the Evangelical Community Hospital in Lewisburg, where he died Dec. 27, aged 73.

Dreibrodt, Ben Allen Ⓜ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1938; veteran of World War II; on the staffs of St. Benedict's, Santa Rosa, and Baptist Memorial hospitals; died in the Robert B. Green Hospital Dec. 22, aged 45.

Fialk, Harry Ⓜ Union City, N. J.; Tulane University School of Medicine, New Orleans, 1929; fellow of the American College of Surgeons; veteran of World War II; on the staffs of the North Hudson Hospital in Weehawken, and the Medical Arts Center Hospital in New York City, where he died Dec. 27, aged 54.

Godfrey, Lincoln Jr. Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1942; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; research director of the National Council on Alcoholism; veteran of World War II; served on the faculty of his alma mater; on the staff of the Presbyterian Hospital; died Dec. 18, aged 43.

Green, Hyman Ⓜ Boston; Harvard Medical School, Boston, 1914; joined the British Expeditionary Forces in World War I and transferred later, as a captain, to the U. S. Army; member of the American Academy of Pediatrics; past-president of the Greater Boston Medical Association, New England Pediatric Society, and the Children's Hospital Alumni Association; associated with Children's and Beth Israel hospitals; died in the Veterans Administration Hospital Dec. 27, aged 68.

Grimes, Ivison, Camden, Texas; University of Tennessee College of Medicine, Memphis, 1914; died Dec. 11, aged 67.

Haight, Vincent Wymand Ⓜ Buchanan, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1919; veteran of World War I; an examining physician for the Metropolitan Life Insurance Company; since 1923 school physician of Central School District No. 3, town of Cortlandt; served as health officer for the village of Buchanan; on the staff of the Peekskill (N. Y.) Hospital; died in the Memorial Hospital, New York City, Dec. 7, aged 63.

Healey, Edward Joseph Gerard Ⓜ Weston, Mass.; Tufts College Medical School, Boston, 1943; veteran of World War II; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology, Inc.; member of the American College of Radiology; radiologist at Waltham (Mass.) Hospital; associate radiologist at the Boston City Hospital; died in St. Elizabeth's Hospital, Boston, Dec. 13, aged 39.

Moet, Joe Louis Ⓜ La Feria, Texas; Baylor University College of Medicine, Dallas, 1941; veteran of World War II; a past-president of the Cameron-Willacy Counties Medical Society; member of the American Academy of General Practice; a member of the school board for the La Feria Independent School District; at one time chief of staff of Valley Baptist Hospital at Harlingen; died Oct. 20, aged 42.

Moore, Neil S. Ⓜ St. Louis; St. Louis University School of Medicine, 1913; on the faculty of his alma mater; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; past-president of St. Louis Medical Society; on the staffs of St. Louis County Hospital in Clayton, St. Anthony's Hospital, and Alexian Brothers Hospital; died Dec. 5, aged 71.

Moreland, James Thaddeus, Idabel, Okla.; Chattanooga (Tenn.) Medical College, 1901; veteran of World War I; died Nov. 22, aged 87.

Nauss, Ralph Welty, Gainesville, Fla.; Northwestern University Medical School, Chicago, 1905; formerly on the faculty of Cornell University Medical College in New York City, where he was on the staff of the New York Hospital; spent three years in the medical mission field in Belgian Congo; author of "Medical Parasitology and Zoology"; died in the University of Florida Infirmary Dec. 15, aged 82.

Northrup, John Fredrick Ⓜ Topeka, Kan.; College of Homeopathic Medicine and Surgery of the Kansas City University, Kansas City, Mo., 1899; died in the Stormont-Vail Hospital, Dec. 7, aged 83.

Owen, Harbert Claude Ⓜ Holly Bluff, Miss.; Memphis (Tenn.) Hospital Medical College, 1902; died in the King's Daughters' Hospital, Yazoo City, Dec. 21, aged 80.

Plaut, Clarence Theodore Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1926; on the staff of the Jackson Park Hospital, where he died Jan. 5, aged 57.

Pontius, Guy Victor Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1923; associate professor of surgery at Northwestern University Medical School; on the staffs of the St. Francis Hospital in Blue Island, St. Luke's Hospital, and Illinois Central Hospital; died Jan. 4, aged 61.

Price, Oscar Jay Ⓜ Somerville, Mass.; Tufts College Medical School, Boston, 1901; for 40 years medical examiner for Metropolitan Life and Prudential Insurance companies; died in the Somerville Hospital Dec. 9, aged 84.

Rife, Dwight William Ⓜ Farmington, N. M.; University of Illinois College of Medicine, Chicago, 1931; interned at the Lutheran Deaconess Home and Hospital in Chicago; veteran of World War I; commander in the U. S. Naval Reserve during World War II and was in the invasion of Okinawa, receiving the Bronze Star as a result of his performance at that time; died Dec. 21, aged 62.

Rock, Thomas Stephen Ⓜ Lancaster, N. H.; Columbia University College of Physicians and Surgeons, New York City, 1947; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; member of the staff and chief of surgery at Beatrice Weeks Memorial Hospital; formerly associated with the Veterans Administration Hospital, White River Junction, Vt.; died in the Mary Hitchcock Hospital, Hanover, Nov. 27, aged 36.

Sachs, Ernest Ⓜ North Haven, Conn.; born in New York City Jan. 25, 1879; Johns Hopkins University School of Medicine, Baltimore, 1904; on the faculty of Yale University School of Medicine in New Haven; professor emeritus of neurological surgery at Washington University School of Medicine in St. Louis, where he was on the staffs of the Ellis Fischel State Cancer Hospital in Columbia, Barnes, St. Louis Children's, St. Louis Maternity, and St. Louis City hospitals; past-president of the American Neurological Association; past-president and secretary of the Society of Neurological Surgeons; member of the Southern Surgical Association, American Physiological Association, St. Louis Surgical Society, Sigma Xi, and Phi Beta Pi; fellow of the American College of Surgeons and the International College of Surgeons; member of the founders group of the American Board of Surgery; specialist certified by the American Board of Neurological Surgery; author of many books; died in the Grace–New Haven Memorial Hospital in New Haven Dec. 2, aged 79.

Schloss, Max Ⓜ Jackson Heights, N. Y.; Ludwig–Maximilians–Universität Medizinische Fakultät, Munchen, Bavaria, Germany, 1924; member of the American Society of Anesthesiologists; died in New York City Nov. 20, aged 60.

Schussler, Edward G. Ⓜ Oaklawn, Ill.; Chicago College of Medicine and Surgery, 1908; associated with Little Company of Mary Hospital in Evergreen Park and the South Chicago Community Hospital in Chicago; died in Chicago Dec. 16, aged 72.

Scibetta, Louis Joseph, Erie, Pa.; Detroit College of Medicine and Surgery, 1928; an associate member of the American Medical Association; died in St. Vincent's Hospital Dec. 17, aged 58.

Segal, Marek M. Ⓜ New York City; Uniwersytet Jozefa Pilsudskiégo, Warszawa, Poland, 1924; associated with the Hospital for Joint Diseases; died in Lake Mahopac, N. Y., Dec. 7, aged 60.

Shoun, Alexander Nelson Ⓜ San Manuel, Ariz.; Jefferson Medical College of Philadelphia, 1932; member of the American Rheumatism Association; president of the Pinal County Medical Society; formerly practiced in Winston–Salem, N. C., where he was school physician with the city department of health; associated with the San Manuel Cooper Corporation Hospital; died Dec. 12, aged 51.

Smith, Clarence B., Roff, Okla.; University of Texas School of Medicine, Galveston, 1899; died in the Valley View Hospital in Ada Dec. 2, aged 82.

Smith, Edward Greer Ⓜ Mercedes, Texas; Dallas Medical College, 1904; for 32 years served the Missouri–Pacific Railroad as local physician; died Dec. 10, aged 86.

Stanka, Andrew George Ⓜ Grand Ledge, Mich.; University of Michigan Department of Medicine and Surgery, Minneapolis, 1909; member of the American Academy of General Practice; served on the staff of the St. Lawrence Hospital in Lansing; died Dec. 13, aged 79.

Strecker, Edward Adam, Philadelphia; born in Philadelphia Oct. 16, 1886; Jefferson Medical College of Philadelphia, 1911; named professor of nervous and mental diseases at his alma mater in 1925, serving until 1931, and in that year became professor and head of the department of psychiatry at the University of Pennsylvania School of Medicine, where he remained in that capacity until he became professor emeritus in 1953; emeritus professor of psychiatry at the University of Pennsylvania Graduate School of Medicine; clinical professor of psychiatry and mental diseases at Yale University in New Haven, Conn., from 1926 to 1932; appointed as the first professor of psychiatry at the Seton Hall College of Medicine and Dentistry, Jersey City; in 1939 was selected to deliver the Salmon Lectures on psychiatry and mental hygiene; gave the Pasteur, Menas Gregory Memorial, and Bernard McGhie Memorial lectures in 1946; specialist certified by the American Board of

Psychiatry and Neurology; an associate member of the American Medical Association; member and past-president of the American Psychiatric Association; member and formerly vice-president of the American Neurological Association; member of the American Psychosomatic Society, the Association for Research in Nervous and Mental Diseases, Alpha Omega Alpha, Sigma Phi Epsilon, and Alpha Kappa Kappa; fellow of the American College of Physicians; on May 24, 1944, received the Dr. I. P. Strittmatter Award of the Philadelphia County Medical Society "in recognition of his distinguished service in the field of psychiatry and mental hygiene and his unselfish devotion to the highest ideals of the profession as physician, teacher, author and consultant in civilian and military medicine"; during World War I held the rank of major in the medical corps of the U. S. Army, as division neuropsychiatrist for the 28th division in France; during World War II named special consultant to the Secretary of War for the Air Forces of the U. S. Army; on Jan. 16, 1948, was awarded the Presidential Certificate of Merit in recognition of his services as consultant to the Surgeon General of the Navy since May 6, 1943; the new building at the New Jersey Neuro-Psychiatric Institute, Princeton, dedicated in 1957 was named after him; since 1917 medical and clinical director of the Pennsylvania Hospital Department for Mental and Nervous Diseases; served as chief of service and consultant at the Institute for Mental Hygiene at Pennsylvania Hospital, consultant to the U. S. Public Health Service, to Bryn Mawr College, and to the U. S. Veterans Bureau; author of more than 200 published papers and several books on psychiatry; died in the Jefferson Medical College Hospital Jan. 2, aged 72.

Tanner, Kirby, Covington, Ky.; Medical College of Ohio, Cincinnati, 1900; died in the Kenton County Infirmary Nov. 8, aged 85.

Thiery, Raymond Donle Ⓜ South Bridgewater, Mass.; Harvard Medical School, Boston, 1923; died in St. Luke's Hospital, Middleboro, Nov. 26, aged 62.

Thompson, Clara Mabel, New York City; Johns Hopkins University School of Medicine, Baltimore, 1920; member of the Medical Society of the State of New York, American Psychoanalytic Association, American Psychosomatic Society, American Psychiatric Association, and the American Psychopathological Association; served as vice-president of the Association for the Advancement of Psychoanalysis; formerly on the faculty of the New York Medical College, Flower and Fifth Avenue Hospitals, and her alma mater; executive director of the William Alanson White Institute of Psychiatry, Psychoanalysis and Psychology; died Dec. 20, aged 65.

Turner, Oliver William Ⓜ Boothbay Harbor, Maine; Jefferson Medical College of Philadelphia, 1893; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; formerly on the staffs of the Augusta General and Augusta State hospitals in Augusta; died in Jackson Heights, N. Y., Nov. 24, aged 90.

Van Horne, Thomas Calvin, Pittsburgh; Medical Department of the Western University of Pennsylvania, Pittsburgh, 1903; an associate member of the American Medical Association; died Dec. 7, aged 83.

Van Tromp, Homer Ovid, Buckhannon, W. Va.; Eclectic Medical College, Omaha, 1913; an associate member of the American Medical Association; past-president and secretary of the Central West Virginia Medical Society; formerly assistant superintendent and clinical director of Weston (W. Va.) State Hospital, where for one year he was acting superintendent; died Dec. 16, aged 81.

Walch, Joseph Francis Ⓜ Lawrence, Mass.; Tufts College Medical School, Boston, 1904; charter member and medical director of the Lawrence Tuberculosis Association; in 1956 awarded a plaque by the Greater Lawrence Tuberculosis Association for his services as medical advisor since 1912; on the staffs of the Clover Hill Hospital, Lawrence General Hospital, and McGowan Memorial Hospital; died Dec. 5, aged 85.

Wapstra, Ilse Sigrid Ⓜ New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1931; died Dec. 29, aged 53.

Ward, William Trulock Ⓜ Salt Lake City; Columbia University College of Physicians and Surgeons, New York City, 1908; for many years on the staff of the Holy Cross Hospital; a member of the board of directors of the First Federal Savings and Loan Association; died Dec. 10, aged 78.

Williams, William Lee, Florence, S. C.; Meharry Medical College, Nashville, Tenn., 1915; died Oct. 1, aged 57.

Willis, James Clinton Jr. Ⓜ Shreveport, La.; Tulane University School of Medicine, New Orleans, 1916; fellow of the American College of Surgeons; president of the Willis-Knighton Memorial Hospital; chairman of the board of directors of Louisiana Bank and Trust Company; senior surgeon for the Illinois Central Railroad; died Dec. 14, aged 67.

Wingquist, Carl Gustave, Crosby, Minn.; University of Minnesota Medical School, Minneapolis, 1932; veteran of World War II; on the staff of the Miners' Hospital, where he died Nov. 4, aged 53.

Wright, Oren Henry Ⓜ Chicago; Rush Medical College, Chicago, 1912; died Dec. 30, aged 73.

FOREIGN LETTERS

AUSTRIA

Operations on the Mentally Ill.—At the meeting of the Society of Physicians in Vienna on Jan. 9, Drs. E. Ringel and H. Schinko stated that a physician is authorized to operate on a patient without the patient's consent if the patient's life is in danger, as in rupture of the stomach. Should the physician establish the diagnosis of a cancer, the operation would also be considered "vitally indicated" inasmuch as the life of the patient is threatened if he is not operated on, but in this case consent of the patient is absolutely necessary. This consent may not be given, however, by a patient with organic dementia, involutional melancholia, amentia, and some types of severe neurosis. Sufficient improvement of the mental disorders, with the exception of some forms of dementia, can be expected today with suitable therapy so that the patient may consent to operation. This year nine patients who had not consented to operation did so after they had been treated at the university neuropsychiatric clinic. These patients are in a good physical and mental condition today. This solution is preferred to operation without the consent of the patient even when he is mentally ill. As to patients with neurosis, the speakers emphasized that their tendency to self-injury may manifest itself in a rejection of an operation or by urging the surgeon to perform an unnecessary operation. In the first instance the psychiatrist should try to persuade the patient to see the surgeon, and in the second instance the surgeon should send the patient to the psychiatrist.

Shorter Hours Requested for Physicians.—The Federal Branch Group of Hospital Physicians have requested shorter hours similar to those already approved for many other professional groups. In letters which were mailed to various hospital managers, attention was called to the enormous work load which has been placed on the hospital physicians and the following demands were listed: (1) a 45-hour week for those hospital physicians who perform their services according to service-agreements with a fixed time of service (up to now, a 48-hour week) in accident-hospitals and in institutions of the District Sick Insurance Funds, (2) every other Saturday off duty, and (3) in hospitals in which, for medical or administrative reasons, a free Saturday every second week cannot be granted, a 10% increase in basic salary.

CANADA

Paralysis Agitans.—DeJong (*Canad. Serv. M. J.* 14:695, 1958) called attention to the difficulty of defining paralysis agitans. Neither the anatomic definition as a disease of the substantia nigra nor the physiological definition as a disorder of the extrapyramidal system is satisfactory. The average physician probably diagnoses the condition on evidence of muscle rigidity and tremor of the limbs, which means that some patients with pulmonary complications due to rigidity of the chest wall or others with neurogenic bladder may not be recorded correctly, and absence of classic features may further diminish the recorded incidence. Canadian Sickness Survey figures suggest a general morbidity for the population of 0.30 per 1,000, rising to 0.85 for the age group from 45 to 64 and 1.52 for those over 65 years of age. DeJong believes that the incidence quoted for the United States of 1,000,000 to 1,500,000 cases is way out of line with Canadian figures. The death rate in Canada for this disease from 1931 to 1956 ranged widely, from 1.42 to 2.49 per 1,000—probably a reflection of the difficulty of accurate diagnosis and recording.

Unlawful Practice Charge.—A charge brought in Ontario of unlawful practice of medicine received a great deal of unfortunate publicity in the press, and the situation was not entirely clarified until the recent publication of an official letter from the provincial College of Physicians and Surgeons in the *Ontario Medical Review*. An English physician was engaged by the Canadian Department of Indian Affairs to treat Indians on an Ontario reservation. For this purpose it was not required that he be licensed in the province (a step which would have involved an internship and examination), provided he treated only Indians of the reservation. Information received by the provincial licensing body indicated that the physician was attending private patients, in spite of a warning to desist, and charging fees. An inspector from the licensing body visited the doctor alleging certain symptoms, received treatment, and was charged $5 for which he was given a receipt on an official government form. A charge was then laid by the inspector of "professing to practice medicine while unregistered under the Ontario Medical Act."

When the case came to court, the Department of Indian Affairs provided defense counsel and one of their officials gave evidence that there was an

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The items in these letters are contributed by regular correspondents in the various foreign countries.

agreement with local physicians, who were overworked, that the government physician could see patients in an emergency and hand over his fees to the government, which this physician had scrupulously done. The magistrate dismissed the charge. In the official statement from the licensing body, the letter indicated that it would not appeal the decision, on the grounds that the case is not of sufficient importance and that its proper function is to place evidence before a court rather than to strive for conviction of the person charged.

Thermal Responses to Drugs.—Medical literature contains confusing reports of the effects of some drugs on body temperature. For instance, it has been suggested that ergot may cause hypothermia, hyperthermia, or no change in body temperature. Shemano and Nickerson (*Canad. J. Biochem. & Physiol.* 36:1243, 1958) have clarified this situation with some experiments on rats given drugs at various ambient temperatures. The drugs investigated included chlorpromazine, ergotamine, Hydergine, *d*-lysergic acid diethylamide (LSD 25), serotonin, and reserpine. They were injected subcutaneously with subsequent hourly recording of the colonic temperature. The room temperature was varied and it was shown that chlorpromazine produced hypothermia at ambient temperatures of 30 to 33 C, no significant effect at 36 C, and hyperthermia at 39 C. Similarly, Hydergine, ergotamine, serotonin, and LSD 25 all caused hypothermia at 25 C and hyperthermia at 33 C. Reserpine caused hypothermia at lower temperatures but no consistent effect at higher ones, and dinitrophenol, a drug usually thought to have a peripheral action on body temperature, followed the pattern of the others. Hence, in assessing the action of a drug on body temperature, it must be realized that there may be a critical ambient temperature at which the effect is reversed. The agents studied appear to interfere with central body temperature regulation.

Tissue Committees.—A recent symposium, reported in *Canadian Doctor* (24:29, 1958) without naming the participants, dealt with the question of whether the hospital tissue committee is worth while. The two basic objectives of such committees are the preservation of the integrity of the medical profession and the protection of patients against needless operations. Such committees lack jurisdiction and are strictly fact-finding bodies giving information to the hospital staff. The gynecologist and the surgeon contributing to the symposium agreed that the committee was necessary in smaller hospitals lacking the censorship imposed by the presence of interns, residents, students, and department heads and thought that its presence also made for a more careful recording of cases. It might also be of value where a colleague was in difficulties because of emotional instability, illness, or too great responsibility. The pathologist urged that evaluation of cases should take place within a matter of hours and that surgeons should not be criticized because of the committee's low rating on a specific type of case. The only value of the statistics was to show comparative trends. The lawyer warned of the legal hazards of condemnation of a surgeon's work by a tissue committee. In a malpractice suit a client's lawyer would be in a strong position if he were aware of such condemnation, and since the tissue committee's reports were hospital documents, they could be subpoenaed. The surgeon should have a chance of explaining to the committee the factors that influenced his decision to operate.

Death Rates and Living Standards.—Metropolitan Life Insurance Company figures show that the death rate in Canada for 1958 was the lowest on record—about 8 per 1,000. This decrease in the death rate reflects in large measure the lower incidence of respiratory diseases and to some extent the lower mortality from chronic diseases in elderly people. Cardiovascular and childhood diseases had a lower rate, and the rate for cancer and motor accidents remained about the same as in 1957. The Salk vaccine helped to reduce the number of poliomyelitis cases to fewer than 300 (mostly in Manitoba) as against 9,000 in 1953. However, as a correspondent in *Canadian Doctor* pointed out, the age-adjusted death rates in both Canada and the United States were higher than in Norway, the Netherlands, and Denmark for males, and the Netherlands and Sweden for females. This correspondent speculated on the paradox that the two countries with the highest standards of living in the world do not keep their citizens alive to enjoy it for as long as persons in slightly less favored countries.

Imipramine in Depressions.—Imipramine or N-3′-dimethylaminopropyl-iminodibenzyl hydrochloride was used to treat 84 patients with dysphoric depression at Verdun Psychiatric Hospital, Quebec, by Lehmann and co-workers (*Canad. Psychiat. A. J.* 3:155, 1958). Their results were roughly comparable to those reported by Kuhn (Switzerland), namely recovery or marked improvement in 30% after two weeks' therapy, and in 60% after eight weeks' therapy. The results were less favorable in patients who had depression associated with neuroses, schizophrenia, or organic conditions than in those with endogenous depression. The dosage usually began at 100 mg. daily by mouth or intramuscularly (both were equally effective) and was increased after a few days to 150 mg. and in a large percentage to from 200 to 600 mg. The incidence of side-effects increased with doses over 200 mg. a day, especially in patients over 65 years of age. The main one was disturbance of autonomic nervous system function, but there were a few cases of toxic confusion, two of epilepsy, and one of mild jaundice.

Acute Alcoholism.—Kofman and co-workers (*Canad. M. A. J.* 79:988, 1958) compared the results of treating 500 patients in a state of acute alcoholic intoxication by giving insulin and dextrose intravenously with those in 163 treated with reserpine and 114 treated with perphenazine. Only a few in the series had delirium tremens. Reserpine was given intramuscularly in 2.5-mg. doses on admission and after one hour and then routinely in six hours, with further doses if the patient remained unsettled. An initial dose of 10 mg. of perphenazine was given intramuscularly and repeated after one hour with subsequent 5-mg. doses as needed. Both reserpine and perphenazine were more effective than the insulin-dextrose regimen, and perphenazine was considered the most effective and least complex agent these workers had used in treating acute alcoholism.

FINLAND

Corticosteroid-Produced Peptic Ulcers.—Heino Laitinen, and co-workers (*Acta rheumatol. scandinav.* 4:205-217, 1958) reported a series of 15 patients with peptic ulcers occurring during corticosteroid therapy which were characterized by a location near the pylorus; large, deep, and often penetrating ulcer niches; mild clinical symptoms; good clinical and roentgenologic healing, even in 7 patients in whom corticosteroid therapy was continued; and absence of late complications, which are not unusual in connection with ulcers at or near the pylorus. The follow-up period was over one year in eight cases, and four years in one. During this time examinations showed an apparently permanent healing. The roentgenograms disclosed either normal conditions or minimal bulbar deformity. Pyloric stenosis, which frequently results from a juxtapyloric ulcer, was not encountered in any of these patients.

Mast Cells in the Gastric Mucosa.—The mast cell count was determined in specimens taken from the fundus of the stomach by the suction biopsy method and reported on by Siurala and Sundberg (*Ann. med. exper. et biol. Fenniae* 36:271-277, 1958). The mean mast cell count in 17 persons with a normal gastric mucosa was 79 ± 8.6. In 8 patients with superficial gastritis it was 125 ± 24.1; in 21 with slight atrophic gastritis it was 153 ± 18.3; and in 11 with severe atrophic gastritis it was 150 ± 13.7. The difference in the mast cell count of a normal and atrophic mucosa was statistically significant. There was also some correlation between the mast cell count and the degree of inflammatory changes. It could not be demonstrated that the age of the patient or the severity of the disease had any definite influence on the mast cell count of the gastric mucosa.

Asian Influenza.—Ohela and Kaipainen (*Nord. med.* 60:1700-1701, Nov. 27, 1958) reported that the Asian influenza epidemic was well started in Finland by the end of September, 1957, but by December the number of new cases began to decrease. The total number of cases was estimated to be at least 700,000. Of the 1,322 persons who died in the epidemic, influenza was the sole cause of death in 478 and in the rest one or more additional diseases were involved. A large proportion of the fatal cases were in patients under 5 and over 65 years of age.

FRANCE

Tomography of the Prostate.—Sichel and Blum (*Journal de radiologie, d'électrologie et de médecine nucléaire*, September, 1958) made tomograms of the prostate by taking negatives at depth intervals of 0.5 to 1 cm. If an adenoma is present, its volume and outline can be determined. In case of cancer, the appearance of the dome of the tumor resembles that of the adenoma but is of greater density.

Deaths from Chloramphenicol.—Lamy and coworkers presented to the Académie Nationale de Médecine a series of three cases of fatal purpura hemorrhagia in children who were given small repeated doses of chloramphenicol. They developed a severe thrombopenia against which corticotherapy was of no avail. The authors believe that the small repeated doses caused the development of an allergic phenomenon. They suggested that unless strong indications exist chloramphenicol should not be prescribed.

Humoral Study of Psychopaths.—G. Sandor and C. Chatagnon studied the serums of 230 psychopathic female patients and reported their results at a meeting of the Académie Nationale de Médecine. Of 43 patients with organic lesions, 11 had a normal serum and 22 had hyper-alpha-globulinemia. The findings in 56 patients with acute depression but no organic lesions were similar. In 24 mentally defective subjects, on the other hand, hyper-alpha-globulinemia was rare but 12 of them had hyper-gamma-globulinemia. The findings in 54 schizophrenics were similar. The authors contrasted the two groups—patients with the organic psychopathy and those with acute depression showing an increase in psychic tension and schizophrenics and mental defectives showing a decrease in this tension. They believed that this tension is associated with a hormonal secretion, which modifies the protein composition of the serum. The neurohormonal action of the anterior lobe of the pituitary may play a part in the production of hyper-gammaglobulinemia, when the nervous tension falls. Gleye and Sandor showed that epinephrine produced in guinea pigs a marked hyper-alpha-globulinemia. It is therefore possible that psychic tension may provoke the secretion of the adrenal medulla.

NORWAY

Primary Dislocation of the Patella.—As a plea for operative instead of conservative treatment for primary dislocation of the patella, Dr. Y. Kjelstrup (*Nordisk medicin,* Dec. 18, 1958) gave an account of nine such patients operated on by him. Serving as informal controls were six patients who, in the same period, had a history of an earlier dislocation of the patella for which no operation had been performed. All of them were much embarrassed by their knees, which in two cases presented marginal fractures. Of the nine primary cases six patients were under 18. Six of the patients came to the hospital with the injured knee flexed and the patella displaced inwards. On operation, inspection of the joint revealed nothing amiss with it apart from the patella and its attachments. The lesions were varied but more or less rupture of the attachment of the vastus medialis tendon was common to all. After suture of the torn structures the knee was slightly immobilized by a bandage which allowed daily inspection and control of the knee. After about a fortnight, movements were permitted, and after three weeks, walking with crutches. With one exception a complete return to normal was achieved.

Nilatil for Angina Pectoris.—At the Aker and Ullevaal hospitals in Oslo, trials were made with nilatil (amino-ethyl-nitrate-p-toluol-sulfonate) in 58 patients who had angina pectoris. Rörvik and Selvaag (*Tidsskrift for den norske lægeforening,* Dec. 15, 1958) reported that this drug is slower to take effect than nitroglycerine, but its action lasts longer—at least two hours. It reduces the systolic blood pressure by 15 to 20 mm. Hg, and its administration can be sublingual or peroral. It is easily soluble in water, and it keeps well for at least a year in tablet form or solution. Within 10 to 15 minutes it provokes a sense of heat and throbbing in the head and, if the dose is big enough, a headache. This headache was the only important side-effect, and it was taken as a therapeutic guide, pushing the dose up to a point just short of the headache level. The usual dosage was one 2-mg. tablet three or four times a day. Headache was a guide to a reduction of the dosage, but there were only two patients in whom headache led to discontinuation of this treatment. As excellent or marked relief of symptoms was obtained in about 67% of their patients, the authors concluded that nilatil was the best slow-acting nitrate derivative available for angina pectoris.

Asian Influenza.—Dr. A. Harboe of the Influenza Laboratory of the State Institute for National Health in Oslo (*Nordisk medicin,* Nov. 27, 1958) reported that the outbreak of Asian influenza started in Rjukan, a small inland town, towards the end of August, 1957. Samples received by his laboratory on Sept. 9 were the first to contain the causative virus. In the middle of September there was an intense outbreak of the disease in army concentrations in Stavanger, and in the course of the next fortnight it spread to most of the military centers in southern Norway. Ultimately the whole of Norway was involved, and 19 different strains were cultivated. The major wave, involving the whole country in the first half of October, was followed by a second wave in Oslo at Christmas. School children and the personnel of military camps showed a particularly high morbidity, and in a camp of 223 recruits 88% were found to have developed antibodies to the virus. In the adult general population in Oslo, the incidence of influenza was between 10 and 15%. After isolation and typing, the different strains were sent to the World Influenza Center in London where they were identified as belonging to the Asian type. In Norway no difference could be found between the Norwegian strains and the prototype Singapore strain in respect to their antigenic properties. Vaccine imported from Denmark and Holland was used in the isolation departments of the larger hospitals. It was calculated that at Oslo's City Hospital vaccination had reduced the number of cases by 50% and the number of sickness days by 60%.

Enuresis.—A note of disillusion over the hospital treatment of nocturnal enuresis was struck by Rinvik and Steel (*Tidsskrift for den norske lægeforening,* Dec. 15, 1958) who treated 186 patients with this condition in a children's hospital. A questionnaire addressed to the parents after discharge from the hospital yielded answers from 122. They showed that a recovery could be claimed in 20%, and some improvement in 17%, whereas in the remaining 63% the enuresis persisted one to six years after discharge. Little use was made of drugs in the hospital where the children were awakened once nightly to empty their bladders. One of the main arguments in favor of hospital treatment for enuresis was the opportunity it afforded for the discovery of organic and mental disease. Various tests were applied, including urography, which in 9 of the 158 patients thus examined showed abnormalities of the urinary tract. There were also 12 cases of men-
50% one or more members of the family also suf-
tal retardation. The 122 answers showed that in
fered from enuresis. The authors concluded that

little can be gained by admitting patients under 5 or 6 years to the hospital even though organic disease can thereby be detected earlier. They are skeptical about the value of reducing the water intake in the afternoon, for the children are quick to circumvent their nurses in this respect. As for drugs, tincture of belladonna continues to have its advocates, but it must be pushed if it is to be effective.

SWEDEN

Radical Pancreatic Surgery.—Erik Millbourn (*Acta chir. scandinav.* 116:1, 1958) performed a radical pancreatectomy on 15 patients with cancer of the head of the pancreas and 1 with cancer of the ampulla of Vater. There were three operative deaths, two of which occurred early in the series. Advanced age (over 70 years) in four patients was not considered a contraindication to this operation. Two patients including one with carcinoma of the ampulla of Vater survived almost four years. Two survived two and one-half years. Two patients felt well and had no signs of metastasis or recurrence when last seen three and one-half and two and one-half years, respectively, after the operation. One patient had a second operation, a pancreaticogastrostomy, in March, 1958, after which he had no evidence of metastasis or recurrence. The average survival time was 23 months. Radical pancreatectomy gave these patients their only chance of survival. The author recommended pancreaticoduodenal resection, combined with the necessary anastomosis, in patients with cancer of the head of the pancreas or of the ampulla of Vater, where local excision via a duodenotomy is not possible. He preferred pancreaticogastrostomy to pancreaticojejunostomy, and stated that total pancreaticoduodenectomy was to be avoided.

The author outlined a two-stage operation, the first stage consisting of cholecystojejunostomy and enteroanastomosis and the second stage, pancreaticoduodenal resection, pancreaticogastrostomy, choledochojejunostomy, and gastrojejunostomy. The gastrojejunostomy must be placed distally to the other anastomosis on the efferent loop. Most of the patients are thus provided with two sphincterless openings for the bile flow to the jejunum, a cholecystojejunostomy established in the first stage and a choledochojejunostomy in the second. The coexistence of the two sphincterless openings for bile flow into the jejunum does not as a rule produce postoperative complications. Of eight patients with two openings one had trouble postoperatively, probably due partly to the fact that one sphincterless opening is all that is necessary for the bile flow to the jejunum. One patient, who subsequently died of peritoneal carcinosis, had attacks of cholangitis in the last months of her life. In patients with carcinoma in the ampulla a biopsy specimen should be taken in the first stage through duodenotomy. In those with carcinoma of the head of the pancreas excision of tissue for biopsy is not always without danger. In addition, it is sometimes difficult for the surgeon to obtain a satisfactory biopsy specimen.

Treatment of Ureterolithiasis.—In 1956 Einar Sandegård analyzed a series of patients with ureteral stones treated expectantly and in *Acta chirurgica scandinavica* (116:52, 1958) he presented a follow-up examination of a similar series five years after the attack. Of these 94% were examined urographically. In the interval of between five and six years from onset to follow-up definite recurrences were found in 17% and probable or possible recurrences in 8%. The roentgenographic follow-up demonstrated a recurrence of renal calculi in only 4%. Thus, although ureteral recurrences were fairly common after ureterolithiasis, concretions were rarely found in the kidney. In all of 86 patients treated conservatively, follow-up urography showed the excretory function of the kidneys to be normal. In 29 treated with active procedures, appreciable renal damage had been present prior to operation in 3 but the remaining 26 showed normal kidney function on urographic follow-up examination. No new lesions such as dilatation of the ureter or renal pelvis were noted.

Combined Tetanus Prophylaxis.—The effect of combined active-passive prophylaxis against tetanus was compared by Bergentz and Philipson (*Acta chir. scandinav.* 116:58-67, 1958) with that of solely passive and solely active immunization by determining the serum antitoxin concentrations in military recruits at different periods after immunization. The effect of a booster dose was compared in the same way in the groups treated with active and combined immunization respectively. The results on 22 subjects with passive immunization only, 19 with combined simultaneous active-passive immunization, and 20 with active immunization only led to the following conclusions: The passive immunity secured by combined treatment was slightly lower than that of passive treatment. Of those immunized passively 60% had titers above 0.2 immunizing units (IU) per milliliter but only 15% of the simultaneously immunized had titers above that level. Corresponding values for the 0.1 IU per milliliter–level were 86 and 68% respectively. Measurable antitoxin concentrations corresponding to active immunity in the serums of those treated with simultaneous prophylaxis appeared later than in those actively immunized. A rise in antibodies was not detected until 45 to 74 days after injection in subjects receiving combined treatment while the rise in antibodies appeared between 14 and 24 days after injection in the group actively immunized. The effect of a booster dose was the same in the group immunized actively and in that treated with a combined injection.

Tennis Leg.—Tennis leg is a traumatic lesion of the calf which is generally believed to be due to a subcutaneous rupture of the plantaris muscle. Arner and Lindholm (*Acta chir. scandinav.* 116:73-75, 1958) questioned whether the signs and symptoms of tennis leg were caused by such a rupture. The location of the pain, the distinct tenderness and hematoma formation on the medial aspect of the calf midway between the heel and the knee, and the loss of power could not be accounted for by rupture of the plantaris muscle belly, its musculotendinous junction, or the tendon itself. Twenty patients with characteristic features of tennis leg were studied. A gap in the medial gastrocnemius belly roughly at the musculotendinous junction was observed in every instance. Surgical exploration in five verified the rupture of the gastrocnemius, while the plantaris tendon was found to be intact in all five. In all 20 patients the rupture was shown to occur on sudden dorsiflexion of a foot in supination and plantar flexion with the knee joint in extension. This combination of movements produces the greatest contraction of the medial gastrocnemius belly thereby exposing it to the greatest indirect violence with resultant rupture.

SWITZERLAND

Exports of Narcotics.—The permanent Central Opium Board (Geneva) drew attention in a report to the obligations of governments in connection with the export and import of dangerous narcotics. Specific reference was made to the West German production of normethadone, a narcotic described as being as dangerous as morphine, and used in such cough mixtures as Ticarda and Taurocolo. This drug is manufactured mainly in West Germany and has been under international control since November, 1954, although Bonn, not being a party to the 1948 protocol, has not exercised any control over it. The West German government failed to report its exports of normethadone for 1957 to the Central Opium Board, although there was evidence that in 1956 preparations of this narcotic had been exported to 56 countries 48 of which did not report the fact when questioned. Some of the governments concerned stated that the importation took place without their knowledge.

The Board blamed the failure to disclose this information on the governments concerned. It strongly recommended that, when any new product for which analgesic or antitussive properties are claimed is about to be marketed, the government of the country of manufacture should subject it to control measures until the World Health Organization has determined its liability to habit formation. The Board stated that the guiding principle in all such cases should be that commercial interests must yield to consideration of public health. After the issue of the Board's report it was stated that the Interior Ministry of West Germany would introduce further legislation for the control of narcotics. The Central Opium Board gave the following data on world narcotics production: In 1957 714 tons of raw opium were produced, less than the average annual production of 867 tons during the period from 1946 to 1957; morphine production was 109 tons, of which 94 tons was used for the manufacture of codeine and other derivatives. The consumption of morphine as such was only 4 tons. The production of codeine was 97 tons, an increase over previous years, of which 90 tons was consumed and the remainder converted into other derivatives.

Of the synthetic narcotics meperidine still leads the field with an annual consumption of 14 tons. The use of cocaine is declining. Annual consumption is now 1,619 kg., a reduction of nearly 400 kg. in three years. The consumption of methadone dropped from 750 kg. in 1954 to 464 kg. in 1957. The Board stated that North America continued to be one of the main destinations of illicit narcotic traffic, particularly in heroin. Much traffic in marijuana occurred in Africa, although attempts have been made to stamp it out in Egypt where several confiscations have been reported. An active illicit drug traffic, particularly in opium, morphine, heroin, and marijuana, occurred in the Near East. In the Far East illicit traffic in these narcotics continued in Hong Kong, Singapore, Malaya, Thailand, and China. There was also illicit opium traffic in Pakistan, India, and Iran.

UNITED KINGDOM

Maple Syrup Disease.—The first British case of a rare disease known as maple syrup disease was observed by Mackenzie and Woolf (*Brit. M. J.* 1:90, 1959). The condition is so called because the urine has the odor of maple syrup. The patient was a 4-month-old girl with anemia, lack of control of head movement, increased muscle tone and tendon reflexes, pallor of the optic disks, a low mentality, and an abnormal electroencephalogram. When the urine was examined to exclude phenylketonuria it was found to smell of maple syrup. On two-dimensional paper chromatography valine, leucine, and isoleucine were found in large amounts. They were also present in excess in the blood, spinal fluid, and saliva. The urine contained large quantities of keto acids and alpha-hydroxy acids, which were responsible for the smell of maple syrup. This was intensified by acidification with sulfuric acid. Further examination revealed the presence of large amounts of indolylacetic and indolyllactic acids. The fasting blood sugar level was only 52 mg. per 100 ml.

Another case was observed simultaneously in New York by Dancis and co-workers (*Brit. M. J.* 1:91, 1959). Maple syrup urine disease is an inborn error of metabolism, involving valine, leucine, and isoleucine and similar in some respects to phenylketonuria, for which it may be mistaken as results of the ferric chloride test are similar for both. In both conditions there is a disturbance of tryptophan metabolism as shown by the excretion of large quantities of indolylacetic and indolyllactic acids. Like phenylketonuria the condition is associated with progressive mental deterioration. Mackenzie and Woolf gave the child a diet low in valine, leucine, and isoleucine, but the mental deterioration was such that improvement was unlikely. They considered that the accumulation of abnormal metabolites, i. e., the hydroxy and keto acids, and the amino acid concentration in the blood were responsible for the mental defect.

Reasons for Shortage of Nurses.—British hospitals are finding it increasingly difficult to maintain a 24-hour nursing service. One difficulty is the provision of adequate night service. The Royal College of Nursing, reporting on the problem, deplored the practice in many hospitals of waking patients at 5 a. m. Because of this, night nurses are expected to do far too much work in the early hours of the morning, and in consequence they suffer from overfatigue and the quality of their work deteriorates. The anxiety associated with night duty causes many student nurses to abandon their careers. The report urged the reduction of night duty from 12 to 8 hours. Other recommendations were two meal breaks away from the wards and advance notice of nights off so that the nurses can join in the social life of the community. Junior nurses should not be left alone when seniors go to meals, and trained nurses should not have to undertake domestic and clerical duties as many of them do at present. Salaries should be adequate. The report recommends that nurses should not do more than two years of continuous night duty.

Air Pollution.—Stocks (*Brit. M. J.* 1:74, 1959) observed that when standardized mortality ratios for bronchitis and cancer in the towns of England and Wales were related to the average amounts of undissolved deposit and smoke from the air, highly significant statistical correlations were found with both types of pollution, after eliminating the effects of population density on the correlations. Data were obtained from 58 towns in the industrial areas of Lancashire and Yorkshire. Air pollution was measured by the "deposit index," or monthly average number of grams of undissolved matter deposited per 100 sq. m. of surface, and the "smoke index," which was measured by drawing a known volume of air continuously through a white filter paper for a given time. The darkness of the stain produced was matched with a standard scale and expressed in milligrams per 100 cu. m. of air. The data were averaged over a period of 10 years. Deaths from bronchitis and cancer of the lung, bronchus, stomach, intestine, rectum, and breast were obtained from the statistical reviews of each area over the last five years.

In all areas examined bronchitis was significantly correlated with atmospheric deposit but not smoke, whereas for lung cancer the reverse was true. In Lancashire lung cancer was strongly correlated with population density and this appeared to confirm the effect of wind-borne smoke on the incidence of the disease. The mortality from cancer of the stomach was related significantly to both deposit and smoke in the urban areas, whereas breast cancer showed no correlation with air pollution. The most likely explanation of this is the exposure of food to dirty air. This view received some support from the fact that in the United States, where the wrapping of food was obligatory long before it was in Britain, death rates from gastric cancer have fallen steadily, whereas in Britain they have not. The correlation of intestinal cancer with atmospheric deposit and smoke was below the conventional level of significance.

Medical Honors.—Included in the list of New Year's Honors are Prof. Arthur P. Thomson, this year's President of the British Medical Association, professor of therapeutics, and dean of the faculty of medicine at the University of Birmingham; Dr. Arthur W. Morrow, physician at the Royal Prince Alfred Hospital in Sydney; and Dr. Milton A. Margai, who has been Premier of Sierra Leone since last summer. A knighthood was also conferred on Prof. A. W. Ewing, director of the department of education of the deaf at the University of Manchester.

Politics in Medicine.—Sir Walter F. Hannay, a Harley Street physician, writing in the *Daily Telegraph* of Dec. 2 deplored the intrusion in the last decade of party politics into the realm of medical science and blamed this intrusion for the present retardation in the advance of medical knowledge in Great Britain. The Imperial Cancer Research Fund, a body supported entirely by voluntary contributions, with no political affiliations, must exist on a meager annual budget of $349,510. This brilliant team of scientific workers has absolute intellectual freedom to pursue its investigations, but is sadly hampered by lack of funds. On the other hand, the government-sponsored Medical Research Council has an annual grant of $61,500,000. The 1955-1956 report of this body covered 270 pages of which 210 were devoted to listing the names of the distinguished scientific personnel and only 56 to the work done during the year. The reported findings of the Council made very indifferent reading, and the taxpayer must speculate on the advantages of so costly an association of research workers. This was cited as one more indication of the paralyzing effect of the politician's encroachment into medical science.

Infant Deaths a Mystery.—Mothers have been blamed unjustly or have erroneously thought themselves at fault when apparently healthy children have been found dead in cots. An expert committee, investigating sudden deaths in infancy, has found them innocent of negligence. A member of the committee, Dr. D. M. T. Gairdner, consultant pediatrician, Addenbrooke's Hospital, Cambridge, speaking at a British Medical Association meeting in Southampton, said no evidence that mechanical asphyxiation played an appreciable part in these deaths was found. This is of great comfort to the mothers. Since the cause of these deaths is still unknown, no suggestions as to their prevention can be given. The inquiry lasted over four years; the sudden deaths of 81 children (53 boys and 28 girls) aged 2 weeks to 2 years, or 23% of all deaths in this age group in the areas studied, were investigated.

If this sample was typical, it meant that 1,600 such deaths occurred in England and Wales yearly. These deaths were rare in infants under 1 month and reached a peak in those of 4 months of age; 58 occurred in the six-month periods between November and April. Only seven babies were found lying face down. Mothers at first said that all the children were perfectly well, but inquiry showed that 11 had been seen by a doctor in the three days preceding death and 54 had had trivial symptoms. Autopsies held after 92 such deaths established the cause in only 23. Both breast-fed and bottle-fed babies were involved. The seasonal incidence supported the theory that infection played some part. Dr. Gairdner concluded that mothers should still be advised not to give babies soft pillows because occasionally babies do bury their heads in the bedding.

The Mental Health Bill.—The government's Mental Health Bill is discussed in an annotation in the *British Medical Journal* of Jan. 10. The Bill appeared about 18 months after the report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency and embodied nearly all the important changes recommended by the royal commission and by the British Medical Association's Psychological Medicine Group Committee. As a result of the detailed examination the bill will receive in Parliament no doubt many minor changes will be made in it, but as it stands it represents a notable administrative advance in the care of the mentally ill. Mental health review tribunals are to be set up in the areas of regional hospital boards to consider applications from patients and relatives for their release from hospital. The single term "mental disorder" is to cover all forms of mental illness or disability, and arrangements can be made for any kind of hospital to receive any type of mental patient, whether on an informal basis or under detention. The bill will remove all the formalities which under the present law must be observed before even a voluntary patient can enter a mental hospital, but, in their own interests or for the protection of others, some mentally disordered patients, as in the past, will be compulsorily admitted to hospital and detained therein.

The four groups of mentally disordered patients who may require compulsory detention are the mentally ill, subnormal, severely subnormal, and psychopathic. The terms "mental defective," "idiot," "imbecile," and "moral defective" will no longer be used. Severe subnormality means a state of arrested mental development which renders the patient incapable of living an independent life. Subnormality means a state of arrested mental development which requires or is responsive to medical treatment. Psychopathic disorder means a persistent disorder of personality which results in abnormally aggressive or seriously irresponsible conduct on the part of the patient and requires or is responsive to medical treatment. Patients may be compulsorily admitted to hospital for observation or treatment. In both cases the application will have to be supported by two medical recommendations, one of these by a psychiatrist.

Whether or not the changes brought about by the bill will be notably and quickly advantageous to patients will depend on the attitude of the public to mental illness. The social adaptation of patients discharged from mental hospitals is often precarious. They and their families can receive much-needed support from the aftercare services provided by the hospital and local authorities, but without education of the general public the way may still be hard for those who are trying to overcome a serious disability.

Opposition to "No Strike" Report.—The British Medical Association Council claims that physicians may, under great provocation, be justified in a mass withdrawal from the National Health Service (NHS). This is often referred to in the lay press as going on strike. This is a misrepresentation of what might, in rare circumstances, happen, because physicians would continue to see patients. Sir Frank Newsam, formerly Permanent Undersecretary of State at the Home Office, was commissioned by the General Medical Services Committee, which is representative of the general practitioners who work in the NHS, to investigate the problems and frustrations of the 22,000 family physicians within the NHS and to suggest other ways in which a health service might be organized. The committee wanted an independent inquiry by someone of some eminence. It forwarded Sir Frank's report to the Council of the BMA and the *British Medical Journal* published it with a statement by the Council in the *British Medical Journal* of Jan. 17. The Council strongly criticized the report, asserting that Sir Frank had completely balked the issue he was instructed to grapple with. Although he failed to suggest any alternative schemes his report is not without value. Its value lies in the warning given to the profession that a "strike" would result in a fully salaried NHS. The Council is at this stage refraining from detailed comment, limiting itself to admitting the value of negotiation and the belief that the medical profession, faced with a serious challenge to its principles and traditions, might be compelled to contemplate withdrawal from the NHS.

Sympathectomy for Hypertension.—Newcombe and co-workers of Leeds (*British Medical Journal*, Jan. 17, 1959) reported a series of 212 patients who underwent sympathectomy for hypertension 4 to 10 years earlier. The operative mortality was 4%. The survival rate of 76% for five or more years agrees with other published records of patients treated by sympathectomy and is in favorable contrast to any published account of a series of patients treated conservatively. A sustained reduction of diastolic pressure of more than 20 mm. Hg occurred in 27%. Retinal improvement occurred in 49% of those with severe changes, and when there was no improvement in advanced retinal degeneration death was not long delayed. Symptomatic relief after sympathectomy was the rule. Reduction of blood pressure, if only for a few months, may prevent malignant hypertension. Sympathectomy in hypertension gives many patients an increased expectation of a full and active life.

Menstruation and Acute Psychiatric Illness.—Investigating the time of hospitalization of 276 women with psychiatric disease Dalton (*Brit. M. J.* 1:148, 1959) found that 46% of admissions occurred during or just before menstruation and that 53% of attempted suicides took place during menstruation; successful suicides were more common during the luteal phase. Of patients with depression and of those with schizophrenia 47% were hospitalized during or just before menstruation. The significance of these figures lies in their prognostic value. Psychiatric patients who first seek advice in the premenstruum may be expected to get worse up to the third or fourth day of the menstrual cycle. Premenstrual tension can be successfully treated whether it occurs alone or in association with psychiatric illnesses and regardless of whether the hormonal changes of menstruation cause or precipitate the onset of an acute psychiatric episode. The influence of menstruation on psychiatric admissions was evenly distributed among single, married, and widowed women; among the nulliparous and multiparous; and among those admitted for first and recurrent attacks. There was, however, a marked difference in age. The disturbing influence of menstruation was greatest among those under 25 years of age. Depressive and suicidal patients were evenly distributed among all ages, while schizophrenia was commonest in the youngest age groups. The remaining patients suffered from a wide variety of psychiatric conditions including psychoses, alcoholism, psychopathic disorders, and neurosyphilis. The dates of their admissions were evenly distributed throughout the menstrual cycle.

Bulletin on Rheumatism.—Family doctors throughout Britain now receive a quarterly report on the latest advances in the treatment of rheumatic diseases issued by the Empire Rheumatism Council. The first of these reports was an introductory document in which Dr. W. S. C. Copeman, chairman of the Council, stated that chronic gout has become increasingly common in the last few years.

Spontaneous Improvement in Psychoneuroses.—In assessing the value of any form of therapy it is important to know the degree of spontaneous recovery to be expected from the untreated patient. Wallace and Whyte (*Brit. M. J.* 1:144, 1959) studied the natural history of untreated psychoneuroses in 49 psychoneurotic patients who would normally have had treatment but for various reasons did not. The patients were classified as recovered, improved, or not improved after follow-up periods of three to seven years. Some improvement was noted in 32 (65.3%). Any recovery that occurred spontaneously did so by the third year. The better-integrated patients showed a higher recovery rate and a greater capacity for adjusting to adverse and difficult circumstances. Factors associated with improvement were a helpful marriage partner, adequate housing, good personality, success in work, general adequacy in life situations, and participation in group activities. This high spontaneous recovery and improvement rate must be borne in mind when assessing the value of any new form of treatment, whether by drugs, psychotherapy, or physical methods.

Zollinger-Ellison Syndrome.—Further cases of the recently described Zollinger-Ellison syndrome were reported by Summerskill and Pender (*Lancet* 1:120, 123, 1959). This syndrome is characterized by *gastric hypersecretion, fulminating atypical peptic ulceration*, and pancreatic islet cell hyperplasia. Diagnosis is usually made retrospectively after gastric operation or at autopsy. Summerskill reported a case diagnosed before operation. The patient had jejunal ulcers and secreted over 500 ml. of gastric fluid hourly with practically no response to histamine stimulation. Acid-pepsin activity was present in the jejunum. Diarrhea and steatorrhea were prominent clinical features. Fat digestion in the jejunum was depressed by the presence of acid, and this caused the steatorrhea and diarrhea. Pender's patient had an islet cell tumor of the pancreas. The patient's daughter also had a benign islet cell adenoma. The patient had had repeated but unsuccessful operations for recurrent peptic ulcers. Eventually treatment by total gastrectomy and removal of the benign islet cell tumor resulted in improvement.

Poliomyelitis Vaccine.—An electron microscope will speed the search for a poliomyelitis vaccine produced without the use of monkeys. This and an analytic centrifuge will be bought by the National Fund for Poliomyelitis Research. Britain and the United States together use nearly 30,000 monkeys a month for producing and testing vaccine, and other countries are entering the production field. Research workers feel that in time the demand for monkeys may outstrip the supply. Each monkey yields about 700 doses of vaccine and costs the manufacturer about $42. There have been difficulties about their export from India, because in some areas monkeys are regarded as sacred animals.

Curtains and Hospital Contamination.—Hughes (*Lancet* 1:152, 1959) studied a 14-bed general surgical ward in an attempt to discover possible causes of wound sepsis. Weekly tests were made from samples of the curtains, which were cotton and of the pull-round type. Staphylococcus pyogenes was isolated from 54% of 250 samples. On one occasion clean curtains, which had been through a high-pressure steam sterilizer, were put up around the bed of a patient who had a staphylococcic wound infection of known bacteriophage type. In less than 24 hours the same bacteriophage type of staphylococci was isolated in large numbers from the curtains.

Health of School Children.—In his report on the School Health Service (The Health of the School Child, Her Majesty's Stationery Office, 1959) Sir John Charles, Chief Medical Officer of the Ministry of Education, stated that one of the main health problems in children is overnutrition and not malnutrition. He blamed too many candies, chocolates, ices, and cookies and too much carbohydrate in the diet. On the credit side, boys and girls are taller, heavier, better clad and shod, and cleaner than they were 50 years ago. They reach physical maturity earlier and may expect to live 20 years longer. Tuberculosis, rickets, and rheumatism in children have been virtually eliminated. Most cases of crippling and deformity are now congenital. More children die from accidents than from disease. Traffic accidents are the cause of half the deaths in children, and many of these occur when children are going home from school. Children should be told about the risk of lung cancer from smoking cigarettes as many school children smoke. An inquiry among 300 boys and girls in a high school on the Isle of Wight revealed that 30% of the boys and 15% of the girls were regular smokers. Increased consumption of candies and chocolate was blamed for the increase in dental decay in children. The school medical service is devoting more attention to emotionally disturbed and delinquent children. The number of children appearing in the juvenile courts has increased in 25 years from 13,000 to 38,000 annually. The school medical service now covers 6,500,000 children in 30,000 schools and more than 2,000,000 have an annual medical examination.

New Deal for Midwives.—The Minister of Health proposed a new deal for midwives to meet the serious shortage in the hospital and private midwife service. Among the recommendations made was the employment by the maternity services of more auxiliary nursing and domestic staff to enable midwives and midwives in training to get on with their professional work. It was also suggested that midwives should have responsibility for individual patients throughout the patients' stay in hospital. New maternity hospitals should be planned with this end in view. Unnecessary rules and restrictions should not be applied to pupil midwives, particularly when off duty, and they should have better opportunities for training than at present. Provision should be made for training women who have no nursing qualifications as midwives. The satisfaction the midwife gets from her work could be increased by inculcating a more appropriate mental attitude in patients and their relatives toward her profession.

Radioactive Fall-out and Leukemia.—An investigation is being carried out by the Lancashire Health Committee into the cause of the reputed increase in deaths from leukemia and aplastic anemia in the district and its possible association with the radioactive fall-out that occurred at Windscale, Cumberland, in October, 1957. A plutonium plant became overheated and quantities of fission products, including radioactive iodine (I^{131}) contaminated the surrounding countryside. It is reported that several young people in the area have died from aplastic anemia. The local health officer is conducting the investigation. All county health officials have been asked to report cases of leukemia and aplastic anemia. Medical Research Council experts think it unlikely that the Windscale accident is linked with deaths from leukemia or aplastic anemia. The major component of the fall-out was I^{131}, which has never been linked with leukemia or aplastic anemia. Neoplastic changes after irradiation do not occur until many years after exposure. As leukemia is rare fluctuations may occur from time to time in any area.

CORRESPONDENCE

ANTIBIOTIC LOZENGES

To the Editor:—In the past few years I have seen a fairly large number of patients who have complained of severe sore throat after using antibiotic lozenges. This was due to infection caused by Candida albicans. In all of these patients the soft palate and pharynx were extremely red. In some there were small white patches indicating the presence of colonies of C. albicans. The pain is more severe in this condition than in that associated with any of the inflammatory diseases of the mouth and throat, including severe streptococcic infections. There have been cases of prolonged illness and even death from this cause. For some time I have questioned the moral and legal right of the manufacturer to market a product so injurious to health and at times to life itself. About 25 different antibiotic lozenges are offered for sale. Some contain more antibiotics than others. At least two are advertised extensively on radio and television.

Following is a list of antibiotic lozenges which are sold on prescription or over the counter in the average pharmacy.

- Single Antibiotic Troches
  - Achromycin pharyngets (Lederle)
  - Achromycin troches (Lederle)
  - Aureomycin pharyngets (Lederle)
  - Terramycin troches (Pfizer)
  - Bacipharyn (Reed & Carnrick)
  - Baci-Troche (Upjohn)
  - Teeds lozenges (Warren-Teed)
  - Pemzoles lozenges (Pitman-Moore)
  - Lozilles (White)
  - Tyrosan lozenges (Recsei)
- Combined Antibiotic Troches
  - Sul-Pondets (Wyeth)
  - Bacillets (Abbott)
  - Pondets, Penicillin-Bacitracin (Wyeth)
  - Candettes (Pfizer)
  - Du-Biotic troches (White)
  - Orobiotic (White)
  - Spectrocin (Squibb)
  - Tracinets troches (Merck, Sharpe, & Dohme)
  - Wybiotic troches (Wyeth)
  - Pentazets troches (Merck, Sharpe, & Dohme)
  - Hydrozets (Merck, Sharpe, & Dohme)
  - Tetrazets (Merck, Sharpe, & Dohme)
  - Isodettes (Isodine)
- *Penicillin G Crystalline* Troches
  - Troches with 5,000; 10,000; 20,000; or 25,000 units each (various manufacturers)
  - Troches with 5,000 units of crystalline penicillin G with benzocaine
  - Troches with 5,000 units of procaine penicillin G

Each of the antibiotic lozenges, regardless of the number used, can permit a Candida infection of the soft palate and pharynx to gain a foothold. If we multiply the several hundred cases which I have seen by the number of family physicians and specialists who have also seen similar cases, the aggregate number and the number of work days lost would be staggering.

The purpose of this letter is to ask what can be done toward a discontinuance of the sale of all antibiotic lozenges. The fact that some physicians prescribe these lozenges cannot be construed as an argument in favor of their use. Many doctors are not aware of the danger involved in using antibiotic lozenges. Unfortunately, few articles have been written by those who have encountered patients with Candida infection of the mouth and throat. Frequently the physician who prescribes the lozenges does not see the patient at the time the severe sore throat develops. Action taken by members of the medical profession could do much to stop this health menace.

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CHLORPROMAZINE JAUNDICE

To the Editor:—I wrote a report on chlorpromazine jaundice, more than two years ago, based on 17 cases (Hollister, *Am. J. Med.* 23:870, 1957); since that time I have seen only one other case. This declining prevalence of jaundice has also been noted by another observer (Pollack, *Am. J. Psychiat.* 113:1115, 1957). To provide further information, questionnaires were sent to 67 psychiatrists and mental hospitals using or investigating tranquilizing drugs; 45 replies were received, providing the following data.

In the year preceding the inquiry, 25 of the respondents had encountered at least one case of chlorpromazine jaundice, while 20 had encountered none. Eighty-seven cases of jaundice were reported by these 25 sources, the largest single series being 13 cases. Data were sometimes incomplete in regard to the number of patients treated for the first time with chlorpromazine during the same period. Available data showed that 70 cases of chlorpromazine jaundice had occurred in about 15,000 patients treated, a prevalence of about 0.5%. Of those respondents expressing an opinion, 20 thought that the recent prevalence of chlorpromazine jaundice was lower than that of their previous experience, and 14 thought that it was similar. None thought that it was higher. The customary practice of most clinicians was to discontinue the drug therapy or switch to another if jaundice occurred; only three continued chlorpromazine therapy throughout the episode of jaundice.

Various reasons were given to explain the lowered prevalence of this complication by those who thought such was the case, the most frequently mentioned reason being that current dosage tended to be lower and better controlled because of prior experience. This reason is contrary to the experience of many investigators that the dosage of drug *bears little relationship to the production of jaundice.* The second most common reason cited was that impurities originally present in the drug had now been removed due to more reliable methods of manufacture. The manufacturer of the compound disclaims this possibility, pointing out that chlorpromazine is a synthetic compound. Also, other phenothiazine derivatives produce similar jaundice, and it is unlikely that all would have the same contaminant. Another idea was that a period of high prevalence of infectious hepatitis could have coincided with the early use of the drug, the latter making patients more susceptible to this illness. Also mentioned were the elimination of patients with known liver disease, the use of alkaline phosphatase determinations as screening during the early phase of treatment, and the fact that many patients may have been previously treated without the knowledge of the physician and thereby "desensitized" to the drug.

Jaundice was reported as a complication of three other phenothiazine derivatives: promazine, mepazine, and prochlorperazine. In the case of the latter drug only one report was received, despite the fact that many of the respondents noted that they were using this drug increasingly. The majority opinion is that chlorpromazine jaundice is a drug allergy. The declining prevalence of this complication with increasing exposure of the population to it is contrary to the usual experience with allergic reactions to drugs. The explanation for this phenomenon is still not clear.

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ELI LILLY MEDICAL RESEARCH FELLOWSHIP (SOUTH AFRICA)

To the Editor:—Medical practitioners who are registered in South Africa and who may at present be in the United States should be aware of the fact that applications may now be submitted for the 1959 award of the Eli Lilly Medical Research Fellowship. The fellowship is for the purpose of research and is not for postgraduate clinical study. The net value of the fellowship is $300 a month for 12 months, plus return traveling expenses to the point of study in the United States of America. Further details can be obtained from the undersigned. The closing date for applications is June 30, 1959.

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MUSEUM OF MEDICAL SCIENCE

To the Editor:—We in the Wellcome Museum of Medical Science have read with great interest the letter by Dr. Frederick Stenn in The Journal (169:67-68 [Jan. 3] 1959). To us has been entrusted the task of maintaining the museum of medical science as a teaching institution designed primarily for postgraduate medical men but suitable, also, for undergraduates, nurses, teachers of biology, and their senior students.

The various aspects of medicine now dealt with in this museum are divided on an etiological basis. Thus, we have eight major heads, namely, protozoal diseases, diseases due to bacteria, diseases resulting from viruses, diseases of rickettsial origin, helminthic diseases, fungus diseases, spirochetal diseases, nutrition and malnutrition, and a small section dealing with venomous snakes and arthropods. The method used to describe these conditions is an elaboration of that devised by the original director of this museum, the late Dr. Daukes. The written matter is presented in a synoptic fashion, illustrated by charts, diagrams, pictures, roentgenograms, gross pathological specimens, and photomicrographs illustrating the histological, pathological, entomologic, and parasitological aspects of the conditions described.

Recently the section of the museum dealing with schistosomiasis was shown at a meeting of the South African Medical Association, in Durban, and the section on trypanosomiasis was on display at the Sixth International Congress on Malaria and Tropical Diseases, in Lisbon. The administrative problems in arranging loans are formidable, a matter well appreciated by all museum curators; but on occasion we have been able to supply some material for use by individuals and institutions who have applied to us for assistance.

We do not fully agree with some of the methods of audiovisual instruction proposed by Dr. Stenn. Some of them go against the ancient axiom that clinical medicine can be effectively learned at the bedside and at the bedside only. We have, however, been much interested to see that the concept of using a museum as a main center for medical teaching has found expression in a letter in The Journal. Changes in medical education evolve but slowly. The example and the potentialities of the system followed in the Wellcome Museum of Medical Science have been increasingly appreciated in the United Kingdom during the 45 years of the museum's existence. We shall be greatly interested to see what developments, if any, may take place in the United States as a result of Dr. Stenn's spirited appeal.

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THE LEISURE CORNER

PART-TIME FARMING

Growing things for profit is not quite the same as growing them for fun, but trying to get a profit out of the soil can provide a great deal of pleasure as a part-time hobby for a physician with an independent income. In part-time farming physicians can get away from the complex problems associated with medical practice and find relaxation in what amounts to a completely different occupation. It is possible to trace concrete accomplishments in farming and to realize a sense of progress and gratification.

A part-time farmer owns his own farm and generally lives on it for at least a part of the year. The farm usually starts off being a place for week-ends and summer vacations. Part-time farming is a quite different and more ambitious procedure than tending a garden about one's home. Actually, many of the problems facing the part-time farmer are similar to those confronting the full-time farmer, with one major difference: the part-time farmer does not depend on his hobby to make financial ends meet.

If you have never worked on a farm it is likely that you have some idyllic notions about the kind of life it affords. Returns are not always up to expectations. When you plan to buy a farm make certain it is in a reasonably accessible location. Investigate all phases of farming with the same perspicacity you would apply to evaluating a medical problem. Your first concern should be equipment. Is your back strong enough to do your own plowing, or should you hire someone else to do it? Do you need one or more horses? What equipment should be purchased and what rented? Do you intend to raise fruit? Do you intend to raise chickens and rabbits? These are some of the questions the part-time farmer must answer. Livestock cannot be neglected; someone must always be on hand to keep a close watch. When arrangements are made it is essential to keep an eye on cost.

If you plan to make part-time farming the profitable hobby it can be, it will be necessary, among other things, to investigate the market for cash crops and determine what crops are adapted to your locale and soil. In this connection, the best procedure to follow is to obtain the advice of neighboring farmers, county agricultural agents, and the state agricultural college. You will probably be told that it is better to raise a small quantity of several crops rather than a plentiful amount of a single one. Then there is always the question of feed; whether to buy it or raise it often depends on how much money is available for this purpose.

If you have read this far and are still intrigued by the thought of part-time farming, you might turn to an excellent book called "Practical Animal Husbandry," by Jack Widmer (Charles Scribner's Sons, 1949). He asserts that anyone interested in farming will be surprised at how quickly it is possible to learn to handle farming problems. The author emphasizes the importance of owning a deep freeze unit and supplies some intriguing information about sheep, hogs, rabbits, turkeys, chickens, ducks, geese, squab, guinea fowl, and beef and about meat processing. He speaks of his farm in northern California, where he has fields of hay, grain, and pasture which supply feed for his animals and a cash income from the surplus.

Many forest products, such as fuel wood, saw logs, veneer logs, posts, pulpwoods, crossties, and piling, can bring ready cash. In certain areas it is possible to grow many types of green nuts, berries, and evergreen trees. Turpentine, maple syrup, and cascara bark can find a market, and should you find yourself with an abundant supply of wild shrubs, there is a demand for them from people who have moved to suburban areas. For those who are attracted to raising bees, only a small investment is required, since bees do not require an abundance of attention.

Although most herbs are grown readily, they, too, must be studied beforehand. Many farmers start out with the six best known herbs, sweet basil, chervil, sweet marjoram, thyme, rosemary, and tarragon; then with more experience one can add the so-called mixers, chive, parsley, and summer savory. When you have become a proficient farmer and have developed a keen taste, similar to that of the gourmet, you can add to your stock anise, caraway, celery, fennel, garlic, and mint. Herbs are the ornamental touches you give to your farm. They can be grown in flower beds, rock gardens, or in special herb gardens situated right outside of the kitchen.

Fur farming is a long-term project and there is no easy route to profit. This specialized type of farming holds a great deal of attraction for physicians, however, especially in the creation of various mutations among fur-bearing animals. Cross-breeding, once begun as a scientific experiment, has grown to be one of the most profitable aspects of fur production. The quickest way to become familiar with the specialized body of knowledge is to visit successful fur farms and talk to the owners. Some states require licenses; therefore, before embarking on the raising of mink or chinchilla, it is best to write to the Department of Agriculture for a list of fur farm associations. You will then be able to learn about breeders, prices, and places to buy stock. Since the fur business is also a fashion business it is advisable to make a study of current fashion trends. At present mink is a most popular item, but one never knows when the fashion cycle will change and fickle fashion turn to another flirting pelt. Other fur-bearing animals are so plentiful, namely beaver, skunk, and muskrat, that there is little point at present in raising these animals for commercial purposes. This would be at best a rather costly bit of amusement.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Serum Cholesterol in an Office Practice. A. I. Josey. J. South Carolina M. A. 54:439-443 (Dec.) 1958 [Florence].

The author made 216 determinations of the serum cholesterol level in 59 patients seen in his private office. There were 57 men and 2 women, all in middle or later period of life. The Bloor method employing the Lietz photrometer was used, and all blood samples were obtained in the morning after a fasting period of at least 12 hours. Twenty-four of the 59 patients did not present any clinical evidence of atherosclerosis. Of these 24 patients, 11 had one or more determinations in which the serum cholesterol level was 250 mg. per 100 cc. or below and 13 had one or more determinations above 250 mg. The remaining 35 patients had definite evidence of one or more of the complications of atherosclerosis. Of these 35 patients, 17 had one or more cholesterol determinations of 250 mg. and above, and 18 had determinations below 250 mg. Eight patients with myocardial infarction fell into the group with serum cholesterol levels above 250 mg. per 100 cc., and 9 cases of infarction occurred in the group of patients with serum cholesterol levels below 250 mg.

Sixteen patients with clinical manifestations of atherosclerosis, who were chosen for their motivation and ability to cooperate, were put on maintenance therapy with a diet low in saturated and hydrogenated fats in conjunction with corn oil, and a preparation of safflower oil containing 80% linoleic acid, in doses of 15 to 30 cc. daily, was regularly prescribed for from 5 to 12 months. The total caloric intake was adjusted in each patient to obtain or maintain an optional weight. These 16 patients had serum cholesterol determinations at intervals of one month or more for a total of 5 to 10 determinations. Twelve of the 16 patients had no significant changes in serum cholesterol levels; 4 patients showed a tendency to a lowered level, but this was not consistent or persistent. The diet, therefore, failed to reduce consistently the levels of serum cholesterol in this group of 16 patients.

The level of serum cholesterol above or below 250 mg. per 100 cc. in single or serial determinations did not reflect the presence or absence of clinical complications of atherosclerosis in the 59 patients. The level of serum cholesterol found at various intervals was quite variable and erratic in presumably normal individuals and in atherosclerotic men, and because of this variability the serum cholesterol level does not appear to be of any value for the prognosis of the development of complications of atherosclerosis.

On the Bradycardic Effect of Reserpine. T. Albano and R. Motta. Minerva med. 49:3904-3909 (Oct. 17) 1958 (In Italian) [Turin, Italy].

The bradycardic effect of reserpine was studied in 38 patients with sinus tachycardia; this condition was due to mitral valvular disease in 8 patients, essential hypertension in 10, chronic cor pulmonale in 4, hyperthyroidism in 5, neurodystonia in 6, and atrial fibrillation in 5. Each patient received an initial dose of 1 mg. of reserpine per day, given intravenously for 4 to 6 days, and a maintenance dose of 0.25 mg. per day, which was continued for as long as the clinical course required it. A return to normal values was obtained within 3 to 5 days in the heart frequency of the 8 patients with mitral valvular disease; subjective symptoms disappeared. The heart action of a 21-year-old woman, who presented tachycardia both at rest and on exertion, dropped within 3 days from 144 to 70 beats per minute, and her general condition improved. Reserpine alone was sufficient to check the marked tachyarrhythmia of one patient with atrial fibrillation; this patient had derived little benefit from previous treatment with digitalis or quinidine. Reserpine was likewise beneficial in 2 of the remaining 4 patients with atrial fibrillation. The pulse rate dropped markedly in the 10 patients with essential hypertension. Good results were obtained in the 4 patients with cor pulmonale: the frequency of the heart became normal, dyspnea disappeared, and cyanosis became more attenuated. Good results were also obtained in the 5 patients with hyperthyroidism and in the 6 with neurodystonia. Side-effects occurred in 2 patients. In one patient with total arrhythmia the treatment had to be suspended because of marked subjective disturbances, which could not be checked by re-

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ducing the daily dose of reserpine; the other patient suffered marked asthenia, which was checked by changing the dose of 1 mg. given intravenously to 0.5 mg. given by mouth.

Familial Occurrence of Congenital Heart Disease: Report of Three Families and Review of the Literature. R. A. Carleton, W. H. Abelmann and E. W. Hancock. New England J. Med. 259:1237-1245 (Dec. 25) 1958 [Boston].

The authors report on 3 families who were studied at the heart station of the Boston City Hospital; among the members of these families 9 with congenital heart disease were found. The first family was composed of the parents and 9 children, and 3 of the latter had congenital heart disease; the second family was composed of the parents and 5 children, and 2 of the latter had congenital heart disease; the third family was composed of 72 members, and 3 sisters and the daughter of one of these sisters had congenital heart disease. One patient in the first family, 2 persons in the second family, and the 3 sisters in the third family had a defect of the atrial septum. Six of the 9 patients with congenital heart disease underwent cardiac catherization; it was this procedure which revealed a defect of the atrial septum in the 3 sisters in the third family, thus permitting the first report of 3 cases with a defect of this type in one family diagnosed by other than clinical means. An additional 141 cases of multiple familial congenital heart disease were collected from the literature, including 4 families with more than one member with a defect of the atrial septum. Environmental gestational factors may sporadically be causative, but the findings in the patients reported on appear to conform best with a single, recessive, autosomal mode of genetic transmission.

Staphylococcal Parotitis. R. G. Petersdorf, B. R. Forsyth and D. Bernanke. New England J. Med. 259:1250-1254 (Dec. 25) 1958 [Boston].

The authors report on 3 men and 4 women, between the ages of 50 and 85 years, with a virulent and hitherto rare form of hospital-acquired staphylococcic parotitis. With one exception, the patients were advanced in age and had severe, debilitating, chronic diseases. In 3 patients, in whom the parotitis was intimately related to a major surgical procedure (cecostomy, suprapubic prostatectomy, or cholecystectomy), the infection within the salivary gland appeared within a week of the operation. In 6 patients the parotitis occurred in the hospital, and in 1 it occurred 2 weeks after discharge from the hospital. Dehydration seemed to be an important predisposing factor and was present in 5 patients. One patient, however, had massive edema. The presence of a tracheostomy tube may have played a part in 2 patients. The clinical picture was characterized by the sudden onset of a firm, warm, erythematous, indurated swelling at the angle of the jaw and over the cheek, associated with fever, local pain, and tenderness and with a high white blood cell count (mean count, 33,000 per cubic millimeter).

Staphylococci were isolated in all patients from the pus released from the orifice of Stensen's duct and were cultured in 6 patients. The organisms were invariably resistant to penicillin, streptomycin, and the tetracyclines; some were inhibited by erythromycin and chloramphenicol; and all were sensitive to neomycin, bacitracin, nitrofurantoin, and novobiocin. Phage typing indicated the presence of an unusually resistant strain (type 80-81) in 3 patients. Five patients survived, and 2 died. Treatment was most effective when antibiotics to which the organisms were sensitive were employed. There was no relationship between the response to treatment and the nature or severity of associated disease. Dehydration and routine prophylactic use of antibiotics should be avoided, since they appear to be the most important predisposing factors in the development of staphylococcic parotitis.

Erythema Infectiosum (Megalerythema): Epidemic in West Germany. H. T. Schreus. Deutsche med. Wchnschr. 83:2165-2167 (Dec. 5) 1958 (In German) [Stuttgart, Germany].

A large number of patients with erythema infectiosum are being seen by general practitioners and industrial physicians and in clinics in West Germany. The symptoms and the course of the disease in the individual patient show that the disease is not new. Epidemics of this skin eruption, which has been designated as erythema infectiosum, epidemic megalerythema, Ringelröteln (ring rubella), large-spotted disease, or simply fifth disease, were reported several times before in Germany. The present epidemic seems to be much more extensive than the previous ones, although exact figures of the incidence of erythema infectiosum cannot be given, since it is not a reportable disease. Another unusual aspect of this epidemic is that the disease is more frequent in women than in children. As regards the nomenclature, the author feels that the term "ring rubella" is inadvisable, because erythema infectiosum has no relation to rubella (German measles).

The disease usually begins in the face or as an enanthem in the mouth, that is, the fauces and the mucosa of the soft palate are somewhat red and occasionally may even show petechial hemorrhages. Spotty outlines on the buccal mucosa and slight redness of the tongue are also observed occasionally. At about the same time, spotty or confluent redness is observed on the cheeks. There may be complaints about itching, moderate headaches, lassitude, and mild sore throat. Increase in temperature is slight. Extension of the eruption from the cheeks to the neck, and from there to the upper arms and wrists, sometimes sparing the elbow region, is rather rapid, as is also the extension to the lower extremities. During the early stage, the eruption resembles that of measles, except that it is somewhat more papular; it is intensely red. The small papular form of eruption usually does not persist until disappearance, but may be followed by large-surfaced, confluent areas of erythema, with relatively sharp but irregular outlines (map-like). The center may become lividly blue, and then dirty brown, whereas the rim remains red, so that at this stage the term "Ringelröteln" may seem justified. The process is not limited to the extremities, for as during the present epidemic the entire body may be involved, even to the palms of the hands and the soles of the feet.

The duration of the exanthem varies; sometimes it is subsiding on the face, while it is still in "full bloom" on the extremities. The etiology has not been completely clarified, but a virus origin is widely accepted. The prognosis is favorable, and no damaging effects on the fetus have been observed when erythema infectiosum occurred in pregnant women. The simultaneous appearance of cases in families and industries is more evident than are successive attacks resulting from contacts. This fact and the favorable prognosis indicate that isolation of patients and closing of schools and factories are unnecessary. As regards treatment, the author recommends only symptomatic therapy, since active therapy might interfere with the immunization processes that are characteristic of the exanthematic diseases.

Histoplasmosis in East Africa. P. E. C. Manson-Bahr. East African M. J. 35:625-629 (Nov.) 1958 [Nairobi].

Histoplasma capsulatum, the organism causing histoplasmosis, is found in 2 forms: (1) the mold-like saprophytic form and (2) the yeast-like parasitic phase. H. dubosii, which is the African form of the Histoplasma organism, is larger in size than H. capsulatum. Infection is caused by the mold phase, which lives in the body as the yeast phase and invades the reticuloendothelial system. Infection is from the saprophytic form in the soil, which has been contaminated by the droppings of birds and bats. The disease does not spread from man to man, but infection takes place from the inhalation or ingestion of dust. Thus, in the epidemiology of this disease enclosed spaces, such as caves, pigeon lofts, and chicken houses, where there is contaminated soil, are of great importance. There are 3 main forms of the disease: the localized form, the generalized disseminated form, and benign pulmonary histoplasmosis. After discussing these 3 forms on the basis of literature reports, the author comments on the incidence of sensitivity to histoplasmin in various regions. Surveys in Africa have shown that sensitivity rates vary from 0 to 17.8% in different parts of the continent, miners from the gold mines of Nyanza province in East Africa showing the highest incidence among miners in Africa. An interesting form of benign pulmonary histoplasmosis in South Africa is known as "cave disease." It was found in members of a speleological society, who had been exploring certain caves in the Transvaal.

Recently a patient with cave disease, the first to be described, from East Africa, came under the author's care. He contracted the disease during an exploration of the Amboni caves near Tanga in Tanganyika. There were many bats, and the floor was covered with guano. The man examined the bat guano closely for insects and ticks. Fourteen days later he started to run a fever up to 104 F (40 C) with rigors and sweats. After the first week the fever began to decline, but was still up to 101 F (38.3 C) when he was admitted to hospital about 3 weeks after the onset of symptoms. Roentgenoscopy of the lungs revealed ill-defined coarse mottlings scattered throughout both lungs. A Friedländer pneumonia or tuberculosis was considered. Later a histoplasmin skin test produced a strongly positive skin reaction to a 1/1,000 dilution. Treatment with penicillin and Chloromycetin had no effect, neither did nystatin and sulfonamides or hydroxystilbamidine and large doses of potassium iodide. The lung mottlings gradually cleared and the cough subsided, but there were still some x-ray changes in the lungs 5 months after infection.

The diagnosis of benign pulmonary histoplasmosis rests upon the history of exposure to bat guano, persistent pulmonary mottlings unlike any other condition, a strongly positive histoplasmin skin reaction, and a positive complement-fixation test. It is unusual to isolate H. capsulatum from this type of patient. Disseminated histoplasmosis should be thought of as a possibility in patients with prolonged pyrexia, with hepatosplenomegaly when leishmaniasis and brucellosis cannot be incriminated. Benign pulmonary histoplasmosis should be considered in diffuse coarse miliary mottlings of the lungs, especially where the Mantoux reaction is negative.

Urinary Tract Infection in Paralytic Poliomyelitis. H. D. Riley Jr. and V. Knight. Medicine 37:281-297 (Dec.) 1958 [Baltimore].

As the result of improved treatment of respiratory failure, there is an increasing number of survivors of paralytic poliomyelitis, in whom factors inherent in severe poliomyelitis and its treatment, including immobilization, urolithiasis, catheterization of the urinary bladder, and possibly antibacterial treatment, may lead to urinary tract infection. The authors studied this form of urinary infection over a 21-month period at the poliomyelitis respiratory center at Vanderbilt University Hospital, Nashville, Tenn. There were 50 patients, of whom 15 entered at the time of onset of acute poliomyelitis, while 33 were admitted 30 days or longer after onset of their disease. Two patients with acute transverse myelitis of uncertain origin have been included in this study. Thirty-five patients were over 15 years of age; 15 were younger. Twenty-six patients were males, and 24 were females. All patients were observed for periods ranging from 2 to 16 months. All but 3 patients experienced persistent respiratory insufficiency, necessitating mechanical aids to respiration. Blood pressure determinations were made at least twice daily on all patients throughout the study. Urine was collected for study weekly, or more often, from all patients regardless of evidence of urinary tract infection. Catheterization was dispensed with, and the urine specimen was collected from the midportion of the uninterrupted stream in a sterile container. The first morning specimen was not used, to avoid the overnight growth of bacteria in bladder urine.

Urinary tract infection was demonstrated in 44 of the 50 patients. It can be assumed that renal tissue damage from persistent or recurrent infections will become a factor of increasing importance in the prognosis of these patients. The disease is characterized by its indolence, frequent lack of urinary symptoms, persistence, and steady progression. Bladder catheterization and general immobilization are important influences in the development of urinary tract infection. Treatment is only slightly effective. A presumed result of frequent use of antimicrobial drugs is a high predominance of Bacillus proteus and Aerobacter aerogenes in cultures of urine. Urolithiasis was present in 21 of the 44 patients with urinary tract infection. Twenty per cent of the patients exhibited persistent diastolic hypertension, which appeared to result from some effect of poliomyelitis other than renal damage by infection.

Variations in the Course of Rheumatoid Arthritis. P. E. Brown and J. J. R. Duthie. Ann. Rheumat. Dis. 17:359-364 (Dec.) 1958 [London].

In previous papers of this series the course of a group of patients with rheumatoid arthritis after admission to hospital was described. Changes in functional capacity and disease activity were considered for the group as a whole. The present communication is concerned with the types of course pursued by individual patients and particularly with the question of whether an appreciable number of patients showed a tendency toward permanent recovery or toward permanent disablement. Functional capacity and disease activity were determined on admission to hospital, on discharge, and at 3 subsequent assessments approximately 2 years apart. Four functional grades were distinguished. Patients with fitness for all normal activity were classified as grade 1; those with moderate restriction of function as grade 2; those with marked restriction as grade 3; and those confined to bed or chair as grade 4. Disease activity was assessed as very active, moderately active, or inactive, according to the erythrocyte sedimentation rate, the hemoglobin level, the presence of signs of inflammation in the joints, and the degree of systemic disturbance.

Studies were made on 247 patients. There seemed to be a tendency for patients to remain at approximately the same functional level for fairly long periods after treatment in hospital; 56% of the patients remained in the same functional grade at the 3 assessments after discharge, and 79% remained either in grades 1 or 2 or in grades 3 or 4. As time went on, a small percentage of patients drifted from the more favorable to the disabled groups. There was little evidence that patients in whom the disease ran the most benign course could be regarded as cured. Of those showing no disability throughout the period of observation, half continued to show signs of disease activity. Only 7% of the total number of patients retained full functional capacity and showed no signs of disease activity after discharge from the hospital. A high proportion of those who were severely disabled still showed signs of disease activity. There was no evidence that in any of these patients the disease had "burned itself out." The prognosis was most favorable in patients who had run a progressive course since the onset of symptoms and had been admitted to hospital within one year of onset.

Tophaceous Gout in a 17-Year-Old Male. K. Davison. Postgrad. M. J. 34:651-653 (Dec.) 1958 [London].

Although tophi are present at the onset of gouty arthritis in 2% of patients, the average time between the onset of gout and the appearance of tophi is 15 to 20 years. In most of the published cases of juvenile gout, tophi were absent or did not develop till the patients were much older. The patient described was a youth of 17 years, who 18 months before admission suddenly experienced pain and swelling in the interphalangeal joints of some of his fingers. Within a few days both ankles and the metatarsophalangeal joints of both big toes were also affected. A diagnosis of acute rheumatism was made, and the patient was treated with bed rest and aspirin. The arthritis slowly subsided over a period of 2 months, but a month later both elbows became swollen and painful and remained so for a month. After an interval of 3 months the ankles, big toes, and elbows were all affected simultaneously for a period of 3 months. Six months before admission the patient had an attack of left renal colic with hematuria. Pyelography revealed no abnormality. At about the same time he was seen by an orthopedic surgeon, who diagnosed rheumatoid arthritis. Shortly afterwards the patient noticed small nodules in his right pinna, over the right patella, and both elbows. Intermittent arthritis continued until his admission to hospital.

Examination revealed white pearly nodules in the right pinna, small subcutaneous nodules over the right patella and the right second metacarpophalangeal joint, and large yellowish nodules in both olecranon bursae, the left one having ulcerated through the skin. Effusions were present in knees and elbows, with pain and limitation of movement. The metatarsophalangeal joint of the right big toe was swollen and red. The blood urea content was 44 mg. per 100 cc., and the serum uric acid was 12.2 mg. per 100 cc. Material from the ulcerated tophus was identified as urate. The patient was treated initially with colchicine by mouth with marked symptomatic improvement. Probenecid (Benemid) was then given orally in a dose of 1 Gm. twice daily, together with a high-fluid intake and a low-purine diet. This treatment was continued, and, apart from a transient recurrence of arthritis, the patient remained symptom-free.

Juvenile gout often differs from adult gout in the absence of classical podagra and the frequent occurrence of polyarthritis. This led to diagnostic difficulty in this patient, but at the time of his admission to hospital the presence of multiple gouty tophi, together with the recurrent acute peripheral arthritis, enabled a clinical diagnosis of gout to be made, which was confirmed by the high serum uric acid level. No family history of arthritis was obtained, and the serum uric acid levels of the available relatives were all within normal limits of 4 to 6 mg. per 100 cc.

Assessment of the Relative Importance of the Allergic, Infective and Psychological Factors in Asthma. D. A. Williams, E. Lewis-Faning, L. Rees and others. Acta allergol. 12:376-395 (no. 6) 1958 (In English) [Copenhagen].

The authors report on 487 consecutive patients with asthma, who attended the asthma clinic of St. David's Hospital in Cardiff, Wales, between 1951 and 1954. There were 274 male and 213 female patients; 248 were children, and 239 were adults. Boys predominated among the children, and women among the adults. Analysis of the causes of asthma in these patients revealed that an infective factor was present in 88%, a psychological factor in 70%, and an allergic factor in 64%. All three factors played a part in the precipitation of asthma in 38%; the infective and psychological factors only played a part in 23%, the allergic and infective factors in 15%, and the allergic and psychological factors in 7%. The infective factor was the only factor causing asthma in 11%, the allergy factor was the sole cause in 3.3%, and the psychological factor was the only cause in 1.2%. The dominant precipitating causes of asthma were the allergic factor in 29%, the infective factor in 41%, and the psychological factor in 30%. Analysis of these causes, as found among the different age groups, suggested that in children up to 5 years of age the psychological factor was the most frequent, and in the group over 45 years of age the infective factor was by far the most important precipitating cause. Supportive evidence of the likelihood of these general observations being correct is given.

SURGERY

Congenital Aortic Stenosis: Clinical and Hemodynamic Findings, Surgical Technic, and Results of Operation. A. G. Morrow, E. H. Sharp and E. Braunwald. Circulation 18:1091-1104 (Dec.) 1958 [New York].

The authors report on 20 male and 10 female patients, between the ages of 4 and 39 years, with congenital aortic stenosis confirmed by the demonstration of a systolic pressure gradient between the left ventricle and a systemic artery. Of the 30 patients, 13 had valvular aortic stenosis, 8 had subvalvular stenosis, and in the remaining 9 patients the obstruction had not been localized. Seven of the 13 patients had anginal pain, 3 had a history of syncopal attacks, and 12 had dyspnea. Only one patient was entirely asymptomatic. Of the 8 patients with subvalvular stenosis, 4 had anginal pain, 2 had histories of syncope, and 6 had dyspnea. Two of the 8 patients were entirely asymptomatic. Every patient had a harsh systolic murmur and a thrill at the base of the heart. A high-pitched, decrescendo diastolic murmur along the left sternal border was also present in 4 of the 13 patients with valvular stenosis and in 4 of the 8 patients with subvalvular stenosis. The second heart sound in the aortic area was diminished in 8 of the 13 patients and in 3 of the 8 patients. Fluoroscopic and roentgenographic examinations of the heart revealed some degree of left ventricular enlargement in all but 3 of the 30 patients. Poststenotic dilatation of the aorta was a prominent feature in almost every patient. Angiocardiography was carried out in 11 patients and always revealed a thickened left ventricular wall and a small left ventricular cavity. Left heart catherization was performed by the transbronchial route in 19 patients. In the other 11 patients, particularly young children, left ventricular pressures were obtained by means of direct puncture of this chamber through the left side of the anterior chest wall. The aortic valve gradients,

i. e., the differences between simultaneous peak systolic pressures in the left ventricle and the aorta or a peripheral artery, ranged from 15 to 172 mm. Hg and averaged 82 mm. Hg. Right heart catherizations were carried out in 28 of the 30 patients; findings suggested encroachment by the enlarged left ventricle on the interventricular septum and right ventricular outflow tract.

Eighteen of the 30 patients were operated on at the surgical clinic of the National Heart Institute in Bethesda, Md. A closed transaortic or transventricular operation was performed on the first 4 patients; surgical intervention under direct vision with the aid of general hypothermia was carried out in the next 11 patients; and the last 3 patients were operated on with the aid of extracorporeal circulation and elective cardiac arrest with the patients at normal temperature. Thus, 14 of the 18 patients were operated on with direct exposure of the aortic valve. Three of the 18 patients died, one of irreversible ventricular fibrillation occurring after the period of inflow occlusion, one of septicemia produced by Pseudomonas organisms 5 weeks postoperatively, and one 10 days postoperatively of massive intrathoracic hemorrhage after the administration of heparin and bishydroxycoumarin (Dicumarol) given in the treatment of femoral thrombophlebitis. The 15 surviving patients are free of cardiovascular symptoms, but despite these gratifying clinical results, postoperative hemodynamic studies in all but 5 indicate that some degree of residual stenosis exists.

Ten years ago congenital aortic stenosis was generally considered to be uncommon and seldom to carry a grave prognosis. The severity of obstruction of left ventricular outflow could not be directly assessed, and suitable surgical procedures for its correction were not available. The changing concepts in respect to this malformation are reflected in these 30 patients. The lesion was found to be relatively common and frequently serious. The severity and site of obstruction could be precisely evaluated, and a physiological basis was provided for the selection of patients for operation providing direct exposure of the aortic valve.

Diagnosis and Treatment of Peripheral Round Infiltrates of the Lung. I. Andersen and B. Clausen. Acta. chir. scandinav. 115:422-426 (no. 6) 1958 (In English) [Stockholm].

The authors report on 52 patients with peripheral round infiltrates of the lung ("coin lesions"), in whom no more than a tentative clinical diagnosis was made and in whom the correct diagnosis was secured by exploratory thoracotomy. Of the 52 patients, 37 were men and 15 were women; 15 (6 women and 9 men) were less than 40 years old, and 37 (9 women and 28 men) were over 40 years of age. Thoracotomy revealed primary or secondary carcinoma in 3 patients (20%), aged less than 40 years, and in 25 patients (69%), over 40 years of age. Tuberculoma was found on surgical intervention in 8 patients (53%), aged less than 40 years, and in 5 patients (14%), over 40 years of age. Of the 52 patients, 17 underwent pneumonectomy; 17, lobectomy; 13, segmental resection; and 5, removal of pleural cysts, hamartoma, and meningocele. There were no operative deaths.

Because of the high incidence of malignant lesions in this series of patients with asymptomatic peripheral round infiltrates of the lung, prompt active surgical treatment is justified. From the form, size, and solidity of the tumor as visualized in plain chest roentgenograms and tomograms, nothing can be deduced except that the hamartomas are perhaps of less regular circular shape than the carcinomas and tuberculomas. The presence of calcification may be suggestive of tuberculoma or hamartoma but does not rule out a diagnosis of cancer. Degeneration may be seen in tuberculoma, in inflammatory processes, and in carcinoma. In most patients bronchography, bronchoscopy, and the study of aspirated bronchial secretion did not provide additional information. Because of the difficulties observed in the preoperative differential diagnosis, extensive use of exploratory thoracotomy is recommended, in the course of which frozen sections of biopsy specimens are subjected to microscopic examination. On the basis of the operative and microscopic findings, the authors determine the type and extent of the operation to be performed.

Clinical Application of a New Flexible Knitted Dacron Arterial Substitute. M. E. DeBakey, D. A. Cooley, E. S. Crawford and G. C. Morris Jr. Am. Surgeon 24:862-869 (Dec.) 1958 [Baltimore].

Since early in 1957 the authors have employed seamless knitted, cleansed but chemically untreated Dacron tubes, in different sizes and in the form of bifurcations as well as multibranch tubes, in the treatment of a wide variety of aortic and arterial diseases, such as occlusive disease of the abdominal aorta and iliac arteries and extensive fusiform aneurysm of the descending thoracic aorta. Analysis of this experience, which now includes a total of 737 cases, reveals results that are, in general, most satisfactory. Although insufficient time has elapsed to provide long-term evaluation of the functional efficacy of these grafts, follow-up observations for periods ranging from 1 to 1½ years have been most gratifying and within this period of time have revealed no failures which could be attributable to the graft. An aortogram made one year after surgical intervention in a patient with extensive arteriosclerotic aneurysm of the abdominal aorta involving the bifurcation and common iliac arteries showed excellent functioning of the bifurcation

Dacron graft used to replace the excised portion with the aortic aneurysm. An aortogram made 14 months after operation in another patient showed restoration of circulation in the right lower extremity by means of a bypass Dacron graft attached by end-to-side anastomoses to the common femoral artery above and to the popliteal artery below.

Moreover, a comparison of these results with those obtained by the authors in their previous experience with other types of synthetic vascular replacements and with homografts indicates the Dacron graft to be superior in all respects. Particularly noteworthy is the fact that the incidence of failure attributable to the graft was significantly less in the Dacron series than in other synthetic grafts. An important factor contributing to the reduction in deaths in the more recent Dacron series is improvement in surgical management resulting from increased experience. The fact remains, however, that the mortality in the Dacron series is significantly lower than in the other series, and this fact, along with the distinctly higher incidence of over-all successful results, provides good evidence of the clinical value and efficacy of the new arterial substitute.

Surgical Complications in a Community Hospital with Particular Reference to Wound Infections. P. J. Guthorn, H. A. Kazmann and Chang You Wu. J. M. Soc. New Jersey 55:650-655 (Dec.) 1958 [Trenton].

The study was begun in January, 1957, at the Monmouth Memorial Hospital in Long Branch, N. J. It was undertaken as part of a surgical residency program. On the ward service, where supervision was possible, an effort was made to search for all complications. Infections on the private service were studied with the cooperation of the attending staff. Two forms were used. One was a Report of Surgical Complications to be filled out weekly on each ward or unit. The responsible house officer checked in the appropriate column. The second was the Wound Infection Report, filled out by the house officer (or, in private cases, by the attending surgeon) and forwarded when the infection had run its course. On the ward service 264 operations were performed, with 15 surgical deaths; on the private service 1,895 operations, with 29 operative deaths. On the ward service a total of 130 complications occurred in 54 patients; forty complications occurred in the 15 ward patients who died within 30 days of operation, and 42 complications occurred in the 29 private patients who died after operation, showing that there is a tendency for complications to be multiple.

The morbidity and mortality on the ward service were higher than on the private service. Factors responsible for the higher incidence of complications on the ward are the greater age, the substantial proportion of patients who are malnourished, and the tendency to seek care late in the course of the disease. Since malnourishment and undernourishment are common among ward patients, a longer time was needed in elective surgery cases to correct nutritional, blood volume, and other disturbances. The tendency to seek medical care late was also evident in the patients admitted, almost moribund, with long-standing intestinal obstruction or chronic blood loss.

A total of 49 wound infections occurred, 16 in the 264 operations on ward patients and 33 in the 1,895 operations on private patients. Frequently the period of clinical quiescence was 10 to 12 days, and in 2 patients 21 and 24 days respectively. The principal offending organism was the hemolytic Staphylococcus pyogenes var. aureus. A total of 69 purulent infections were studied bacteriologically. All were mixed infections except for a few of the face and neck. The hemolytic Staph. aureus was present in 45 of these and the nonhemolytic Staph. aureus in 32. In smaller numbers the following organisms were found: Pseudomonas aeruginosa, Proteus vulgaris, Bacillus subtilis, Escherichia coli, nonhemolytic Staphylococcus albus, diphtheroids, Clostridium organisms, and hemolytic and nonhemolytic streptococci.

There were many gaps in the bacteriological study; for instance, phage typing either was not available or was not done in sufficient numbers to demonstrate a connection between the organisms encountered in the hospital and those in the wound infections. There was evidence that the incidence of wound infections appears to be increasing, and that wound infections tend to occur as small epidemics. There was a higher incidence of antibiotic resistance in the hospital infections, although the flora of both in-hospital and out-of-hospital infections are similar.

Primary Adenocarcinoma of the Appendix: Report of 16 Cases. Acta chir. scandinav. 115:447-456 (no. 6) 1958 (In English) [Stockholm].

The authors report on 9 women and 7 men with primary adenocarcinoma of the appendix. Thirteen of the 16 patients were over 50 years of age, 1 was 48 years old, and 2 were less than 40 years of age. The cases of these patients, who were treated at various Danish hospitals, were recorded at the Danish Cancer Registry in Copenhagen between 1943 and 1956. Most of the patients had clinical manifestations of appendicitis. Appendectomy was performed on 7 patients. Of these, 3 are still alive, without signs of recurrence, 2, 4, and 10 years after the surgical intervention. One patient died of peritonitis one week after the operation, and the remaining 3 died of recurrence 9 months, 2 years, and 3 years after the operation. Four patients were subjected to appendectomy followed by right-sided hemicolectomy after the lapse of 5, 19, 53, and 193 days. Three of these are still alive, without signs of recurrence, 21 months, 2 years, and 4½ years after the first admission. The fourth patient, who underwent hemicolectomy 6 months after the appendectomy at a time when cutaneous metastases in the operative scar had occurred and there was macroscopically visible recurrence at the site of the appendix, died of recurrence 12 months later. Of the remaining 5 patients, 2 died in the hospital after palliative surgical measures for ileus; 3 were not operated on, 2 of them being admitted in hopeless condition and dying within a few days and 1 dying of an abdominal tumor and ascites within 2 months after admission. In all the patients, the diagnosis of adenocarcinoma of the appendix was made only at operation or autopsy. Histologically the tumors showed the same structure as cancers of the colon.

Adenocarcinoma of the colonic type is the rarest and most malignant form of carcinoma of the appendix. The diagnosis cannot be made preoperatively but is established often as a surprise, by microscopic examination. Appendectomy can be regarded as adequate treatment only when the lesion is confined to the mucosa and is of peripheral localization; in all other cases, right-sided hemicolectomy is indicated. Recovery from malignant mucocele of the appendix may be achieved by appendectomy, provided that rupture of the appendix has not given rise to peritoneal pseudomyxoma. If this has occurred, as much as possible of the gelatinous material must be removed; if the cecum shows involvement, hemicolectomy must be performed. In the presence of a carcinoid tumor, which occurs about 10 times as frequently as carcinoma, appendectomy is sufficient.

Indications for Open Heart Surgery Using Temporary Cardiopulmonary Bypass. D. A. Cooley. J. Louisiana M. Soc. 110:407-410 (Dec.) 1958 [New Orleans].

Cooley reviews observations on 465 patients who, during the past 2½ years, were operated on with the aid of a pump oxygenator which permitted open cardiotomy during temporary cardiopulmonary bypass. Among these patients, who were treated at several hospitals in Houston, Texas, there were 392 with congenital and 73 with acquired lesions. The over-all mortality among the 164 patients operated on for ventricular septal defects was 18%. Age was an important factor in survival, the operative mortality being 40% among patients less than 2 years old and 7% among 100 patients ranging in age from 2 to 15 years. Since no deaths occurred in patients with normal or moderately elevated pulmonary arterial pressure, the author feels that almost all ventricular septal defects should be repaired.

Of the 123 patients with atrial septal defects, 90 had the ostium secundum type. The 6 deaths in this group concerned patients more than 25 years old and usually with advanced cardiopulmonary disease. The majority of patients less than 25 years old should be operated on if a significant left-to-right intracardiac shunt is present. Twenty patients with ostium primum defects were operated on, with 3 deaths. Seven deaths occurred in the 13 patients with canalis atrioventricularis communis. This complicated anomaly may be virtually incorrectible, but in many instances a satisfactory repair may be obtained.

Twenty-nine patients were operated on for the tetralogy of Fallot. In the acyanotic or minimally cyanosed patient with the tetralogy of Fallot, the results were comparable to the results in isolated ventricular septal defect. Among patients exhibiting severe cyanosis and diminutive pulmonary artery, the operative mortality was 40%. The author says that, in very small infants in critical condition from cyanotic spells, the anastomotic procedures of Blalock and Potts offer palliation. Risk of operation is low in congenital aortic and subaortic stenosis, 20 patients with this defect being operated on without a single death. Among 22 patients operated on for pulmonic valvular and infundibular stenosis, one died. Excellent results are obtained with open heart surgery in these lesions. Of 10 patients operated on for total anomaly of pulmonary venous drainage, 7 survived. The 3 deaths occurred in patients with complicating features making any form of surgical attack extremely risky. Complete repair was achieved in 3 patients with aorticopulmonary septal defect.

In 6 patients with transposition of the great vessels, surgical correction with use of the pump oxygenator was not successful. Poor results were obtained also in 15 patients with miscellaneous congenital defects, such as mitral atresia, single ventricle, tricuspid atresia, truncus arteriosus, and Ebstein's disease.

Those with acquired lesions who underwent open heart surgery included 24 with calcific aortic stenosis. The results of operation on these patients were encouraging. Regarding mitral stenosis, the author says that division of the commissures under direct vision permits accurate repair of the mitral stenosis and control of thrombi and embolism from the left atrium. This technique was used in 10 patients, all of whom had previously undergone closed commissurotomy. The procedure, which at present is reserved only for the recurrent lesions, may later be used for primary operations. All 4 patients subjected to operation for ventricular aneurysm after myocardial infarction survived with good functional results. Treatment was successful in 3 patients with cardiac myxoma. Good results were obtained also in 3 patients with stab wounds or blunt injuries of the heart.

Abdominal Repair of Hiatal Hernia: A Study of 138 Cases. E. S. Crawford and M. E. DeBakey. Am. Surgeon 24:889-895 (Dec.) 1958 [Baltimore].

The authors report on 138 patients with hiatal hernia who were treated surgically at the Jefferson Davis, Methodist, and Veterans Administration Hospitals in Houston, Texas, between 1951 and 1958. There were 72 men and 66 women, but, if the patients treated at the Veterans Administration Hospital are excluded, there were more women than men. The ages of the patients ranged from 32 to 85 years, with more than 33% being over 60 years of age. The transthoracic approach was used in 24 patients and the abdominal in 114. The transthoracic route was used in most of the early cases, but during the past 4 years this approach has been employed only in patients with other thoracic lesions. The increasing preference for repair of the hiatal hernia by the abdominal route has been caused by frequent association of the hiatal hernia with other lesions, such as cholelithiasis, duodenal ulcer, and leiomyoma of the intestine. In patients with such associated lesions, the latter may be surgically treated at the same time that the hernia is repaired if the abdominal route is employed. There were 57 abdominal lesions associated with hiatal hernia in the 114 patients subjected to abdominal repair; in addition, appendectomy was performed on 47 patients, gastrostomy and digital esophageal dilatation on 9, and bilateral lumbar sympathectomy on 1.

The technique employed for the abdominal repair of the hernia included an upper abdominal midline incision and exposure of the hiatal region by retraction of the liver medially and the stomach downward. Retraction of the stomach downward reduced the hernia and permitted exposure of the hiatus through an incision in the peritoneum between the esophagogastric junction and the diaphragm. This exposure was completed by encircling the esophagus with umbilical tape for traction and dissecting the retroperitoneal fibrofatty tissue from the lateral margins of the hiatus. The hiatus was reduced to normal size by approximating the lateral margins behind the esophagus and suturing the esophagogastric junction to the under surface of the new esophageal opening.

Two of the 138 patients died, and these 2 deaths occurred among the patients treated by transthoracic repair; one was due to myocardial infarction, and the other to disruption of the diaphragmatic incision. Hiatal hernias recurred in 2 patients subjected to thoracic repair and in 4 subjected to abdominal repair. Symptoms, such as burning pain, vomiting, regurgitation, hematemesis, melena, dysphagia, belching, and nausea, were relieved in all patients who had successful abdominal repair; however, of 3 patients subjected to thoracic repair, 2 later required cholecystectomy and 1 required gastrectomy for relief of symptoms. The effectiveness of the technique employed in the abdominal repair of hiatal hernias was evident in the extremely low incidence of recurrence (3.5%) and the safety with which it was combined with other abdominal procedures.

Adenomas of the Adrenal Cortex. M. M. Desyatov and M. G. Trachtenberg. Khirurgiya 34:35-41 (no. 10) 1958 (In Russian) [Moscow].

Modern methods of examining patients with endocrine diseases, such as suprarenopneumography, determination of urinary 17-ketosteroid concentration, and the cortisone test, facilitate the diagnosis of adrenal cortical adenoma. The authors present 20 case reports of patients with the Itsenko-Cushing syndrome. The patients were subjected to lumbotomy and excision of the tumor. The operation was carried out with the patient under oxygen-ether or spinal anesthesia. To prevent suprarenal insufficiency, the patients were treated preoperatively with preparations derived from the adrenal cortex—corticotropin (ACTH) and desoxycorticosterone acetate. Cortin and cortisone were given during the postoperative period. Two patients died. A stable positive effect was observed in the rest of the patients, and the clinical symptoms of this disease gradually disappeared. Women treated by this method began to menstruate again. Excessive hair on the face, body, and extremities disappeared. These women reduced in weight, their arterial blood pressure became stabilized, and they experienced no headaches or general weakness.

Contributions to the Pathological Anatomy of Thrombosis and Embolism. A. I. Strukov and N. N. Vasilieva. Khirurgiya 34:86-96 (no. 10) 1958 (In Russian) [Moscow].

The authors present a statistical analysis of thrombosis and embolism for 20 years (1938-1957), based on data of the department of pathological anatomy of the Sechenov Medical Institute in Moscow. Fourteen thousand eight hundred fifty-three autopsies were performed during that period, and 128 embolisms of the pulmonary artery (0.86%) were recorded. The incidence of this complication rose in the years between 1940 and 1954 from 0.91 to 3.92% but was totally absent during the war period (1942-1945). This confirms the observations of foreign authors. The rise in the incidence of thromboembolism of the pulmonary artery coincides with the increase in the percentage of tumors and diseases of the cardiovascular system as the cause of death. The distribution of thrombosis and embolism among different nosological forms demonstrated that the first place is occupied by diseases of the cardiovascular system, constituting 56% of the thromboses and 37% of all the thromboembolisms of the pulmonary artery. The incidence of thrombosis and embolism among patients with tumors of various localizations appeared to be lower than among those with diseases of the cardiovascular system. The absolute number of thromboses and embolisms in the group of tumors is still high (26% of all thromboses, 38% of all thromboembolisms of the pulmonary artery). The veins of the lower extremities, the right heart (especially the right auricular appendage), and the veins of the small pelvis constitute the source of thromboembolism of the pulmonary artery. The authors recommend the use of anticoagulants in the treatment and in the prophylaxis of thromboembolism of the pulmonary artery.

Modern Therapy of Blood Coagulation Disturbances. D. M. Grozdova and V. A. Agranenko. Khirurgiya 34:101-108 (no. 10) 1958 (In Russian) [Moscow].

The use of anticoagulants in surgical clinics has a pronounced therapeutic effect in the acute and subacute stages of thrombosis and thrombophlebitis. In the treatment of acute thrombosis and of thrombophlebitis, the most rational method is the administration of preparations of the heparin and coumarin groups. The most effective method of treatment, which makes possible prevention of recurrence of the disease and of various complications, is the surgical treatment of thrombophlebitis. Anticoagulant therapy is indicated after surgical treatment of thrombophlebitic splenomegaly, portal hypertension, and diseases in which splenectomy or vascular anastomosis is required. This therapy decreases the danger of postoperative thrombosis. Intravenous injection of heparin is most effective in acute stages of thrombosis. Intramuscular injections of heparin at intervals of 6 to 12 hours prolong its action. Prolonged anticoagulant therapy is indicated in the recurrent form of thrombophlebitis of the extremities and in patients with a history of myocardial or pulmonary infarction. This treatment is conducted under control of the prothrombin concentration (65-80%). The authors' observations of such prolonged therapy (from 2 months to 2 years) showed the absence of recurrence of the disease or of untoward side-effects due to the administration of the anticoagulant drug.

Hematological Changes After Total Gastrectomy. W. Kothe. Beitr. klin. Chir. 197:184-191 (no. 2) 1958 (In German) [Munich].

Total gastrectomy was performed on 59 of 1,083 patients with carcinoma of the stomach at the Karl Marx University of Leipzig between 1945 and 1956. The 40 patients who have survived from 1 to more than 4 years have all required special care, because, with total loss of the stomach, metabolic as well as hematological changes can be expected. Literature reports on blood changes after total gastrectomy are mentioned, and the author describes studies of iron metabolism, by means of iron tolerance tests, on 21 patients on whom gastrectomy had been performed up to 4½ years previously. There was evidence that iron resorption becomes impaired after total gastrectomy.

Total loss of the stomach generally produces hematological changes, which progress in phases from hypochromic anemia to megalocytic anemia of half-pernicious character to true pernicious anemia. The time of appearance of each phase differs, as it is not entirely dependent on the duration of absence of the stomach. After a patient has survived total gastrectomy for 3 years, the blood picture (the peripheral and the bone marrow punctate) should be examined at intervals of 3 months, because the author found that the development of pernicious anemia may take place within a few months.

Surgico-Angiological Problems in Diabetes Mellitus. G. Meyer-Burgdorff and E. Kricke. Beitr. klin. Chir. 197:139-151 (no. 2) 1958 (In German) [Munich].

The authors are concerned with whether the vascular lesions of diabetes mellitus represent a special form of angiological disease. The question is raised whether the metabolic disorder or the treatment with insulin is the decisive factor in the pathogenesis. Although specific diabetic changes in the structure of the vascular walls have not been demonstrated, numerous factors have been cited to show that "diabetic angiopathy" does represent a special form. It is characterized by premature sclerosis, particularly of the terminal vessels, and the resulting stasis leads to secondary changes in the conveyor arteries. The capillary damage, as a rule, appears only after the diabetic disorder has existed for from 5 to 15 years, but sometimes very severe forms of vascular disease are observed in young diabetic patients. Although some investigators include only nephropathy (Kimmelstiel-Wilson disease) and retinopathy in the concept of "diabetic angiopathy," others also include gangrene of the extremities, and this last form is of particular interest to the surgeon. The authors cite figures to demonstrate the high incidence of gangrene of the extremities in diabetics.

In discussing the influence of insulin on the blood perfusion of various tissues, the work of several investigators on this problem and that of one of the authors are cited. The observed increased blood perfusion of the muscles of diabetics indicates increased capillarization, and the blood perfusion of these capillaries is further increased by insulin. The increased blood perfusion of the muscles apparently is at the expense of the blood perfusion of the skin. Deficient circulation in the skin, however, is likely to cause necrosis and gangrene, and since insulin acts chiefly on the muscles, it may be regarded as indirectly responsible for gangrene, rather than as having a retarding effect on the development of that condition.

Since exclusion of the sympathetic system promotes the blood perfusion of the skin, the authors advocate sympathectomy for the prevention of diabetic gangrene. They report their observation on 61 diabetic patients with vascular complications in the extremities. Twenty-two of 42 patients who had received conservative treatment and 10 of 19 who had been subjected to sympathetectomy required subsequent amputation, that is, the same percentage in both groups. However, taking into account the level of the amputation, it was found that, whereas 80% of the amputations after conservative treatment were extensive, only 33% of those after sympathectomy were extensive. This indicates that sympathectomy in diabetics during the stage of necrosis shifts the level of the amputation in the distal direction. The authors advocate sympathectomy as a prophylactic measure against gangrene of the extremities in diabetic patients.

Multiple Hemangiomas of the Jejunum as a Cause of Massive Gastrointestinal Bleeding.

A. L. Evans, O. S. Cofer and H. H. Gregory. J. M. A. Georgia 47:600-603 (Dec.) 1958 [Atlanta].

The authors cite figures from the literature, which prove the extreme rarity of hemangiomas of the small intestine, and present the history of a male patient who had had no intestinal bleeding until he was 61 years old. When hospitalized at age 63, in July, 1957, this patient complained of epigastric discomfort and bleeding from the rectum. He stated that approximately 2 years prior to admission, while at stool, he passed large amounts of bright red blood through the rectum. He became so weak that he fainted. After that time, at about 2-month intervals, he had other similar episodes. He had been thoroughly examined by several physicians and at 2 university clinics and was told that all x-ray, sigmoidoscopic, and fecal examinations were negative. He was advised to have an exploratory laparotomy but refused. Eight months prior to admission he began to have constant epigastric pain of a burning nature, which radiated under his ribs and sternum. He was treated for this with a bland diet and antacids with little relief. The pain had become progressively worse and was constant day and night. It had no relation to meals but was aggravated by deep breathing or stooping over. After thorough examination the patient was told that the cause of bleeding could not be located and was advised to have an exploratory laparotomy. On the 5th day after admission he had severe melena and consented to surgical exploration.

The small intestine was explored first, and at the ileocecal area and along the ileum small bluish nodules were noted. As the jejunum was approached, these became more numerous. The proximal jejunum was studded with numerous bluish nodules, varying in size from 3 to 16 mm. (matchhead to size of a dime). Examination of the stomach, liver, colon, and other abdominal viscera failed to reveal further tumors. It was decided to resect only the proximal part of the jejunum in the hope that the bleeding had arisen from the larger tumors; the proximal 90 cm. of the jejunum, beginning 3 cm. distal to the ligament of Treitz, was resected. An end-to-end jejunojejunostomy was done. The postoperative course was uneventful. Examination of the specimen disclosed that the background of the bluish nodules was that of cavernous hemangiomas in the submucosa. There was no evidence of malignancy. The patient experienced further hemorrhages, requiring blood replacement after the operation. Since the entire small intestine cannot be removed, it was hoped that another look might uncover the chief area of bleeding or that multiple mural excisions could be considered.

The commonest presenting symptom of multiple hemangiomas of the small intestine is bleeding from the rectum. A few cases have been reported in which there was intestinal obstruction or intussusception, and occasionally inflammation of the tumor simulated appendicitis. In some cases, these intestinal hemangiomas cause only vague abdominal symptoms. Large hemangiomas may be diagnosed preoperatively by characteristic phleboliths in the roentgenogram. The diagnosis is usually made by exploratory laparotomy or at autopsy. Repeated melena with unexplained anemia or numerous hemangiomas of the skin should arouse suspicion of intestinal hemangioma. The patient presented had a hemangioma on the lip. Hemangiomas should be considered before doing a "blind" gastric resection. The treatment is surgical; results are excellent in single lesions, poorer in multiple lesions.

Cause of Death in Surgery of the Newborn: Emphasis on Prevention of Aspiration.

R. Spencer. J. Louisiana M. Soc. 110:418-422 (Dec.) 1958 [New Orleans].

This report is concerned with 74 infants, less than 1 month of age, who in the course of the last 3 years were observed on the pediatric surgery service of the Charity Hospital of Louisiana in New Orleans. Twenty-eight of these 74 infants died. This study includes all the infants who were operated on, or whose condition was diagnosed as being a surgical one, on or before the 30th day of postnatal life. Twenty-one of 37 infants with early congenital anomalies died. Their average age at operation was 4 days. More than half of the deaths were due to pulmonary complications—atelectasis and pneumonitis. The anomalies in this group were congenital obstructive lesions of the alimentary tract, perforation of the stomach as a result of an abnormality in development, omphalocele, Siamese twins, and multicystic kidney. There were no deaths among the 17 patients with late congenital anomalies, which included pyloric stenosis, incarcerated inguinal hernia, and Hirschsprung's disease. The average age of these infants was 23 days.

All 6 infants with noncongenital emergencies early in the neonatal period died. This group included 2 infants with paralytic ileus due to sepsis, a 9-day-old, 900-Gm. (2-lb.) baby with a bleeding gastric ulcer, and 3 1,400-Gm. (3-lb.) infants with a condition labeled constipation-dehydration. These dehydrated patients apparently died of intestinal obstruction produced by plugs of inspissated milk curds. At autopsy there was increased fibrosis in the pancreas of one of these patients. All 3 infants treated for trauma survived. The only death among 11 infants with miscellaneous conditions concerned a 3-week-old baby with a cystic hygroma of the axilla, who had diarrhea, then pneumonia, and finally died of viral hepatitis and septicemia due to Escherichia coli 13 days after operation.

The deaths due to multiple congenital anomalies were mostly unavoidable, but the largest group of deaths, those due to pulmonary complications, should be preventable. The most important factor in prevention of death from aspiration is early diagnosis and treatment of congenital obstructive lesions of the alimentary tract. Any infant who is difficult to resuscitate at birth or who has intermittent cyanosis and excessive mucus should be suspected of having atresia of the esophagus with tracheoesophageal fistula until the diagnosis has been excluded by passing a catheter through the esophagus and into the stomach. Every newborn infant who vomits, particularly if the vomitus contains bile, should be subjected to roentgenoscopy of the abdomen to rule out congenital intestinal obstruction. If tracheoesophageal fistula with esophageal atresia is suspected because of inability to insert a nasogastric tube, the diagnosis should be confirmed by fluoroscopy.

Once the diagnosis of intestinal obstruction is made, x-ray studies with contrast material are contraindicated. The infant should be placed on his abdomen, and decompression of the gastrointestinal tract should be undertaken. In these small patients the ordinary urethral catheter is superior to the Levin tube. Gravity drainage and intermittent aspiration of the catheter with a syringe are preferable to strong constant suction. Preoperative decompression of the gastrointestinal tract cannot be overemphasized. Frequent suction of the nasopharynx is almost as important in intestinal obstruction as in tracheoesophageal fistula. Newborn infants have poor cough reflexes and many aspirate the increased secretions resulting from the irritation of the nasogastric tube. Additional preoperative measures for both tracheoesophageal fistula and intestinal obstruction include minimal but adequate hydration, transfusion if necessary, antibiotics, and administration of an adequate drying agent before induction of anesthesia. The smaller the infant, the more important is this last measure.

Postoperatively, all these patients require an atmosphere of high humidity, suction of the nasopharynx, and the prone position. Even with the most expert nursing care, these tiny patients, who have poor gag and cough reflexes, will often aspirate secretions—usually with disastrous results. For this reason, gastrostomy is recommended in congenital intestinal obstruction.

NEUROLOGY & PSYCHIATRY

Horse Serum Neuropathy. A. A. Marinacci. Bull. Los Angeles Neurol. Soc. 23:149-159 (Dec.) 1958 [Los Angeles].

This study is concerned with electromyographic studies on 115 patients who had muscular paralysis in the region of the shoulder girdle and arms. These patients had received serum therapy in the form of tetanus antitoxin for lacerations or deep wounds. Electromyographic studies demonstrated that this horse serum plexitis can be misinterpreted and that other disease entities have been falsely incriminated. This results because the disorder has a latent period of from 6 to 12 days after the injection of antitoxin. When the paralysis appears a week or 2 after the injection, the serum therapy has usually been forgotten. Another important fact is that the paralysis usually is focal and may involve either a group of muscles supplied by a single peripheral nerve or the group of muscular structures innervated from the fifth cervical nerve root or an isolated peripheral nerve such as the axillary nerve.

Electromyography proved valuable not only in revealing the true nature of this neuropathy but also in differentiating it from other diseases. Electromyographic studies revealed more widespread involvement than did the clinical signs. It was found that the roots and trunks of the brachial plexus are rarely involved and that its cords are only occasionally affected. The damage is largely limited to the proximal peripheral nerves which have their immediate origin from the roots of the brachial plexus, such as the dorsal scapular and long thoracic nerve of Bell, from the trunks, such as the subclavian and suprascapular nerves, or from the cords, such as the medial and lateral anterior thoracic, subscapular, thoracodorsal, axillary, and musculocutaneous nerves. The terminal branches of the cervical plexus are also affected, while the radial, median, and ulnar nerves are rarely involved directly. Occasionally involvement of either the radial, median, or ulnar nerves may be seen. However, the involvement in these nerves is due to pressure on the nerve while the patient is in bed and not due directly to the horse serum itself. The most commonly affected nerve is the axillary, next the suprascapular, then the musculocutaneous, the cervical plexus, and the long thoracic nerve, and finally the dorsal scapular.

This neuropathy resembles several other conditions, particularly anterior poliomyelitis, cervical cord tumor, amyotrophic lateral sclerosis, cervical cord trauma, cervical nerve root compression, a lesion of the upper trunk of the brachial plexus, shoulder-hand syndrome, and finally cerebral vascular accident. The peripheral effects of this disease entity are further substantiated by its favorable prognosis for complete recovery from the paralysis. It is the author's opinion that this disease should be designated as a horse serum neuropathy rather than as a horse serum "plexitis," because the plexus per se is not involved in the majority of instances. Finally, because horse serum neuropathy stems from trauma, the electromyogram makes clear its relationship to an industrial as well as a medicolegal prognosis, especially when the patients are observed for as long as 3 years.

Routine Blood Control on Permanent Treatment with Mesantoin and Dimedion. E. Kjøboe and E. Kroman. Nord. med. 60:1599-1602 (Nov. 6) 1958 (In Danish) [Stockholm].

In 59 patients treated with Dimedion and in 110 treated with Mesantoin, the treatment was usually started during hospitalization and continued after the patient was made ambulant. Leukocyte and differential blood counts were carried out 2 to 4 times a month during the first 2 months, then, as a rule, once monthly. In view of the grave prognosis in granulocytopenia, patients treated with substances which can cause this complication should be given reasonable safety. In 3 cases of granulocytopenia, with 200 or fewer granulocytes per cubic millimeter, originated during treatment with Mesantoin or Dimedion, the granulocyte count had gradually diminished during the preceding weeks. Routine blood control at 4-week intervals is believed essentially to increase the chance of demonstrating a beginning granulocytopenia. In many cases an apparently harmless granulocytopenia will be found, with spontaneous remission, but such a finding should always occasion repeated blood cell counts at short intervals if administration of the preparation in question is continued. Clinical observation and instruction of patients as to the symptoms in severe granulocytopenia (fever, sore throat, tendency to abnormal bleeding) are necessary but not sufficient, since a severe granulocytopenia can appear without clinical symptoms. Treatment with Mesantoin and Dimedion should be introduced only when other antiepileptics have been tried.

Hydrosaline Disorders in Familial Periodic Paralysis. M. Espinar Lafuente, A. Sánchez Agesta, J. Díaz Nogales and E. de Landázuri. Rev. clín. españ. 71:86-92 (Oct. 31) 1958 (In Spanish) [Madrid].

A man, 26 years old, was hospitalized at the medical clinic of the University of Granada, requesting treatment for recurrent crises of familial periodic paralysis from which he had been suffering for the past 6 years. The paralytic crises were more or less severe, involving mainly the legs and to a moderate extent the arms and being associated with nausea and vomiting. They subsided within 24 hours, leaving a sensation of great muscular weakness in the limbs. The clinical and biochemical examination of the patient in the periods when he was free from these attacks gave normal results.

In studying this patient, an artificial paralytic crisis was induced by the intramuscular injection of desoxycorticosterone acetate (DOCA) which was administered at 12-hour intervals in doses of 10 mg. per injection up to a total of 5 injections. The crisis appeared 9 hours after the 5th injection of DOCA. It lasted 30 hours, after which the sensation of muscular weakness was reported by the patient. The stage of induction of the crisis lasted 6 hours (2 before and 4 after paralysis was established). It was marked by hypopotassemia, hypernatremia, and abundant diuresis, the urine containing a large quantity of sodium. The sodium-potassium ratio was high and became still higher during the peak of paralysis which lasted 24 hours. This stage was marked by a progressive lowering of sodium and potassium blood levels, the sodium returning to a normal value and the potassium to a still lower figure. Recovery was marked by profuse diuresis, with a large quantity of sodium in the urine and a moderate amount of potassium. The sodium-potassium ratio was increased, with the potassium blood level returning to normal. This stage was prolonged for several hours after termination of the crisis. Normal elimination of potassium in the urine and normalization of the sodium-potassium ratio occurred on the second day after termination of the crisis. Calcium and creatinine in the blood were at normal levels.

The authors believe that their observations in this case, and those previously reported in the literature, confirm the fact that crises of familial periodic paralysis are due to disorders of the metabolism of electrolytes and water, with consequent primary sequestration of potassium in the cells of the skeletal muscles and secondary sequestration of sodium.

Suicide and the Medical Community. J. A. Motto and C. Greene. A. M. A. Arch. Neurol. & Psychiat. 80:776-781 (Dec.) 1958 [Chicago].

The authors investigated the degree of contact that suicidal persons had with the medical community, before making a suicide attempt, in 175 consecutive suicides and in 197 unsuccessful suicide attempts in San Francisco between November, 1956, and September, 1957. At least 74 (42%) of the persons who committed suicide and 116 (60%) of those who attempted suicide were under medical care or had been so during the 6 months preceding the suicidal act. The physicians involved in the reports of the 372 persons represented all major medical specialties, except pediatrics; psychiatrists, general practitioners, and internists accounted for 47% of the 227 physicians known to have treated these patients. The patients complained most frequently of nervousness, depression, insomnia, abdominal distress, headache, apprehension, and seizures. Routine postoperative follow-up and antepartum and postpartum care also demanded attention as situations preceding a suicide attempt. Of the 372 persons, 84 (23%) had been in touch with a physician for at least a month before the suicidal act. Fifty-nine persons (16%) committed the act within a week of the last medical contact, and 14 (4%) had done so on the same day the physician was seen. Another 147 persons (40%) had seen a physician within 6 months of the suicidal act. Thus, the medical community is seen to be extensively involved in the suicide problem. The degree and kind of contact between members of the medical community and suicidal persons, and especially the physician's anxieties about suicide, are suggested as factors that should be studied further in assessing the physician's role in suicide prevention.

Psychic Symptoms in "Asia Disease." F. Askevold and A. Skulstad. Tidsskr. norske laegefor. 78:1066-1067 (Nov. 1) 1958 (In Norwegian) [Oslo].

Eight cases are described in which the psychiatric illness, for which the patient was admitted, seemed to develop after an acute febrile disorder in the fall of 1957, regarded as Asian influenza. In 4 patients episodes of mental symptoms had occurred previously, and hence the Asian influenza was considered as a precipitating factor. In 2 patients with protracted convalescence antibodies against the virus of Asian influenza could not be demonstrated. In 2 patients there was evidence of encephalitis, with marked schizophreniform symptoms.

GYNECOLOGY & OBSTETRICS

Chlorothiazide in Edema of Pregnancy. R. Landesman, R. N. Ollstein and K. J. Quinton. New York J. Med. 59:66-70 (Jan. 1) 1959 [New York].

Chlorothiazide (Diuril) was given to 100 pregnant women with edema in the toxemia clinic of the New York Lying-In Hospital. Of the 100 patients, 17 had preeclampsia, 27 had chronic hypertension without superimposition of acute toxemia, 16 had superimposition of acute toxemia, and 40 were normal. The drug was administered orally in doses ranging from 0.5 to 1.5 Gm. per day, the usual amount being 1 Gm. per day, given in divided doses of 0.5 Gm. The first tablet was given on arising and the second tablet in the afternoon so as to afford the patient an uninterrupted sleep, since the diuresis was then usually completed before retiring. The usual course of therapy was 7 days. However, some patients received chlorothiazide daily for several months. In rare cases administration of 1 Gm. of the drug per day produced nausea sufficient to require reduction in dosage to 0.5 Gm. per day with subsequent disappearance of symptoms. When diuresis did not follow the administration of 1 Gm. of chlorothiazide per day, the dose of the drug was increased to 1.5 Gm. per day. Seventeen patients received 1 mg. of reserpine daily, together with chlorothiazide. Four patients received 250 mg. of acetazolamide (Diamox) per day for one week.

All the patients responded to chlorothiazide with an initial weight loss, most marked during the first week of therapy. In the presence of clinically detectable edema, the agent was universally effective. The response was about proportional to the amount of edema initially present. Some patients showed an initial weight loss, but on prolonged therapy the diuretic response lessened, and a gain in weight occurred. In most patients diuresis diminished on sustained therapy when an apparent low-weight level was reached. Further increase in dosage had no effect in promoting diuresis. None of the patients accumulated massive edema fluid while receiving the drug. The patients with uncomplicated chronic hypertension showed a significant drop in blood pressure in response to chlorothiazide. The combination of chlorothiazide and reserpine appeared to enhance the hypotensive effect. With the onset of an acute process the antihypertensive effect of chlorothiazide was negligible when at all present. Chlorothiazide did not display apparent ability to reverse the toxemic process, since it did not reduce either fetal loss or the incidence of small babies. Chlorothiazide is a safe, potent, orally administered diuretic. The optimum daily dose is 0.5 Gm. given twice daily. On a balanced low-salt diet, chlorothiazide may be administered for periods up to 4 months without significant toxicity resulting to mother or fetus.

Problems in Diagnosis and Causes of Hirsutism. M. J. Fairweather and J. W. Goldzieher. J. Am. M. Women's A. 13:501-509 (Dec.) 1958 [New York].

The classification of the causes of hirsutism in women presented by the authors lists 4 principal groups: (1) adrenal causes, which include hyperplasia and adenoma and carcinoma of the adrenals; (2) ovarian causes, which include (*a*) different masculinizing tumors, such as arrhenoblastoma, adrenal rest type (masculinovoblastoma), hilus-cell Leydig-cell tumor, and luteoma and (*b*) the Stein-Leventhal syndrome; (3) familial form of hirsutism, without recognizable endocrine disorder; and (4) iatrogenic form (induced by androgen therapy). To explain the endocrine basis of hirsutism in adrenal hyperplasia, the authors discuss the mechanism of the pituitary-adrenal axis. They also mention the newer techniques of urinary steroid studies and the range of 17-ketosteroids under normal conditions and in the various conditions that may lead to hirsutism.

To illustrate situations that may be observed in the differential diagnosis of hirsutism, the histories of 6 patients are presented. The first patient, a 33-year-old woman, had adrenal cortical hyperfunction (Cushing's syndrome) with marked hirsutism. Adrenalectomy was performed on the left gland, and a gray encapsulated tumor, measuring 10 cm. in diameter, was removed. Histologically, the tumor cells resembled those of the adrenal cortex. Five months after the operation the patient felt well, and since then has given birth to 4 living infants. In the second patient, in whom hirsutism resulted from an adrenal rest tumor of the ovary, a large (8 by 8 cm.), pedunculated, nodular tumor of the left ovary was removed. The third patient had the Stein-Leventhal syndrome, showing round face, beard, and extreme degree of frontoparietal baldness. At operation, the uterus was found to be 3 or 4 times the normal size, and the ovaries appeared large and cystic. The uterus, tubes, and ovaries were removed. Under ordinary circumstances, that is, in the absence of uterine carcinoma, wedge resection of the ovaries is usually sufficient in the large majority of women with the Stein-Leventhal syndrome.

In the fourth patient, a 60-year-old woman, exploration of the pelvis revealed a pedunculated fibroid on the uterine fundus and an intramural fibroid on the right side of the fundus. The ovaries were bound down, small, and atrophic. After myomectomy a bilateral salpingo-oophorectomy was done. The patient bled briskly, and the blood pressure fell but was restored with levarterenol bitartrate. As the bleeding could not be controlled, a hysterectomy was performed. The patient was discharged from the hospital on the 9th postoperative day. Microscopic sections revealed a small ovarian tumor nodule, composed of small lobules containing oval-to-round hyperchromic and vesicular nucleated cells with light gray to pink cytoplasm. These were diagnosed as Leydig-cell rests. The history of the fifth patient, a 25-year-old woman, illustrates the difficulties encountered in making the diagnosis of familial hirsutism. This patient had a family history of excess hair growth and, although showing some menstrual disturbance, gave evidence of ovulation. On the basis of urinary steroid studies, the authors conclude that a mild degree of adrenal hyperplasia was present, superimposed on a strong family history of hirsutism. The sixth patient had adrenal hyperplasia that responded to cortisone therapy.

Primary Cancer of the Vulva. Ann. chir. et gynaec. Fenniae (supp. 5) 47:17-29, 1958 (In English) [Helsinki].

A series of 182 patients with primary carcinoma of the vulva were treated at the Institute of Radiotherapy, University of Helsinki. The patients were classified into 2 groups: one consisted of 153 patients who had not received treatment prior to their admission to the institute, and the other consisted of 29 patients who had had treatment at another hospital. The patients of the first group presented different stages of the disease; in one-fourth of the patients it was too widespread to attempt any therapeutic measure. Several patients of the second group had cancer, grade 1. Relapses and metastases occurred in more than one-half of the patients. Of the 153 patients belonging to the first group, 116 were amenable to treatment, and 98 of these were subjected to local electrocoagulation. The inguinal lymph nodes were treated by means of teleradium therapy or roentgenotherapy in two-thirds of the patients, but no such treatment was applied to this region in the remaining one-third. The 5-year survival rate was 36.1% among the 98 patients who were subjected to electrocoagulation, 27.5% among the 153 patients who had had no treatment before admission, 42.1% among the 145 treated patients, and 60.5 to 65.5% among the patients with cancer, grade 1. In addition to electrocoagulation, other local treatments, such as surgical extirpation of the tumor, treatment by means of a radium plate or by intubating radium needles, teleradium therapy, or roentgenotherapy, have also been used. This study illustrates the importance of early treatment of patients with carcinoma of the vulva, which constitutes no exception from other types of carcinoma.

Formal Carcinogenesis in the Uterine Cervix. H. G. Hillemanns. Arch. Gynäk. 191:235-270 (No. 3) 1958 (In German) [Munich, Germany].

The formal genesis of beginning tumor growth is just as problematical as is its causation. The question whether certain tissue changes are neoplastic or preneoplastic is of fundamental importance for the evaluation of the surface carcinoma of the uterine cervix. It is closely allied to two other questions, namely, whether this cancer must be traced to unicentric germination of the tumor anlage or to multicentric foci, and whether one is to expect a monophasic or a polyphasic growth. The author traces the various steps in the formal carcinogenesis in the uterine cervix. He himself performed all histological studies on material obtained from the clinic and from a cancer detection center in connection with colposcopic and cytological studies at the women's clinic of the University of Freiburg. In the course of the 5 years from 1953 to 1957, studies were made on 84 surface carcinomas, 24 microcarcinomas, and 638 cervical carcinomas in stages 1 to 4 (including microcarcinomas); also in 30 cases with unstable epithelium and in 26 with atypical epithelium, cases which are being watched and are still inconclusive.

The simultaneous appearance of surface carcinomas with erythroplasia, as well as similar local conditions on the external female genitalia, justifies the classification of surface carcinoma as a precancerosis. With exact observation, multicentric development can be demonstrated in 25% of the cases. In the majority of cases carcinogenesis is a unilocular process at the epithelial border of the cervix. Multiple genesis corresponds to the results of experimental cancer production and coincides with the field theory described by Willis in 1944-1945 and in 1953. The author mentions the possibility of the appearance of multicentric foci, as well as the misinterpretation of recurrences and metastases.

The tumor anlage is of multicellular origin; this is proved by multicentric foci and varying types of carcinoma on adjoining matrixes. Whether further dissemination takes place only by proliferation or also by inductive modification is still being discussed. As is proved by the study of microcarcinomas, the growth of true cancer originates from several sites of the preneoblastic surface epithelium, that is, it is pluricentric. Experimental tumor formation takes place in several phases and resembles a gradual dedifferentiation. Biphasic growth can be proved in cervical cancer as it has been in the dermatological precanceroses.

Biological studies demonstrated that the transition from the normal-appearing to the cancerously degenerated cell takes place gradually over a period of time, not in sudden leaps; the process can be followed morphologically. Cancer formation in the cervix is likewise a chronic process with prolonged latency. However, after a certain threshold value has been reached, infiltration occurs in a short time. On the basis of his own experiences and of the critical evaluation of previous reports, the author believes that, as regards the cervix, the morphologically monophasic carcinoma, developing directly and without latency, is without significance. Spontaneous regressibility of a surface carcinoma (established on the basis of strict criteria) does not seem to have been proved, and can be expected only after a change in the milieu.

The author emphasizes the decisive importance of the method of securing and processing tissues for the evalution of the growth of cervical carcinoma. After commenting on pathological and gynecologic viewpoints, he assumes a gradual increase in the malignancy in cervical carcinoma, in accordance with the biphasic mechanism in experimental carcinogenesis and with the demand for multiple cancer cells for tumor formation. In Druckrey's scheme of precancerosis, surface carcinoma is defined as the early stage of a malignant process which is still of purely cellular character.

Detergents in the Treatment of Leukorrhea. P. Godts. Belg. tijdschr. geneesk. 14:1085-1092 (Nov. 15) 1958 (In Flemish) [Leuven, Belgium].

According to Godts, detergents are widely used in the treatment of leukorrhea resulting from vaginal infections. He defines detergents as substances capable of reducing the surface tension of water, and discusses their characteristics. After describing the isolation of Candida albicans from the vaginal smears of patients with leukorrhea, he reports studies on the effects of various solutions of the detergents, Sabenyl and Neo-Sabenyl, on cultures of C. albicans isolated from such smears. The therapeutic use of detergents consists in, first, cleansing the vagina with a tampon containing a detergent solution; then a tampon that has been saturated with 5% solution of detergent is inserted into the vagina and is left in place for from 12 to 24 hours; this is followed by daily vaginal irrigations with a detergent solution for one week.

The 90 patients with leukorrheal vaginitis, treated with detergents and reviewed in this paper, included 30 with infections due to C. albicans (which are especially frequent in pregnant women), 30 with trichomoniasis, and 30 with mixed infections. Although the importance of Trichomonas vaginalis as a cause of infection has not been definitely established, when these parasites disappear from the vagina secretions after treatment, the clinical symptoms subside. The term "mixed infection vaginitis" was applied when either, both, or neither of C. albicans and T. vaginalis are found together with bacterial organisms. Treatment with detergents produced excellent results in 71 of the 90 patients—in 26 of those with moniliasis (C. albicans), in 24 of those with trichomoniasis, and in 21 of those with mixed infections. Good results were obtained in 9 additional patients (including 5 with mixed infections), whereas in the other 10 patients the effects of treatment with detergents were poor. On the basis of these results, the author recommends the use of detergents in the aforementioned forms of leukorrheal vaginitis.

Clinical Significance of the Enzymatic Study of the Ascitic Fluid in Maligant Tumors of the Ovary. G. Santoni. Minerva ginec. **10**:677-681 (Sept. 15) 1958 (In Italian) [Turin, Italy].

The author studied the lactic dehydrogenase activity in the ascitic fluid of 15 women with malignant tumor of the ovary, in 10 women with no tumor, and in some normal women. The values of this activity in the ascitic fluid of the 15 women with ovarian tumor were much higher than the values obtained in patients without tumor and in the normal women. The author believes that the lactic dehydrogenase activity is the result of the enzyme present in the necrotic parts of neoplastic tissue. The high lactic dehydrogenase activity, in fact, was present in patients with malignant tumor of the ovary already in an advanced stage. The values of the lactic dehydrogenase activity in the blood serum of women with malignant tumor of the ovary were found to be lower than the values of this activity in the ascitic fluid; therefore, the author believes that the enzyme present in the ascitic fluid does not derive from the blood.

The Conservative Operation for Endometriosis: A Report of Its Use in 200 Cases. L. A. Gray. J. Kentucky M. A. **56**:1219-1225 (Dec.) 1958 [Louisville].

The author reports on 200 women, between the ages of 18 and 40 years, who underwent the conservative operation for endometriosis. One hundred fifty-three patients (76.5%) were less than 30 years of age. Forty-seven patients were unmarried, 153 were married, and 28 (18.3%) of the latter had had children previously. The chief complaints of the patients were dysmenorrhea in 86.5%, sterility in 50.5%, intermenstrual pelvic pain in 33%, menometrorrhagia in 32.5%, and dyspareunia in 25.5%. One hundred twenty-nine patients (64.5%) had retroversion of the uterus. The conservative operation for endometriosis is a distinct one in gynecology, including dilatation of the cervix and curettage, excision of endometrial implants, resection of endometrial cysts, and suspension of the uterus. The approach was through a midline incision. Presacral neurectomy was performed in 44 patients (22%) who had the more severe dysmenorrhea. Myomas were excised in 31 patients. Modified Gilliam suspension of the uterus was performed on 178 patients.

There were no deaths and no obstructions. Subsequently 57 of the 200 patients became pregnant. Of 49 patients specifically complaining of sterility, treated in the past 10 years, 25 (51%) became pregnant. The relief of dysmenorrhea, pelvic pain, dyspareunia, and menometrorrhagia was gratifying. Six of the 200 patients have had secondary radical operations. The conservative operation for endometriosis requires care, tedious dissection, and often more time than hysterectomy. The results obtained confirm the impression that this operation is a satisfactory and proper method of treatment when it is strictly indicated because of disabling symptoms or because of sterility which does not respond to usual conservative procedures. It should not be performed though, until the patient has been observed and surgical intervention seems clearly necessary. In case of realization and necessity of a second laparotomy later, the conservative operation for endometriosis should not be considered a failure if normal health has intervened for a number of years or if pregnancy has occurred.

Delay by Physician and Patient in the Diagnosis and Treatment of Pelvic Cancer. C. E. Flowers Jr., R. A. Ross and N. L. Pritchett. South. M. J. **51**: 1497-1504 (Dec.) 1958 [Birmingham, Ala.].

According to the American Cancer Society, 50% of those who die of cancer could be saved if patients and physicians would familiarize themselves with and use all available knowledge of the disease. During a 4-month period 191 patients with pelvic cancer were studied at the North Carolina Memorial Hospital in Chapel Hill to determine the preventable factors in their disease. The charts of 70 of these patients who died of pelvic cancer were also reviewed. The incidence of delay on the part of the physician to give a proper diagnosis, and of delay on the part of the patient to consult a physician after the occurrence of the first symptoms of pelvic cancer, was established according to the Philadelphia Plan for Pelvic Cancer Control. It was evident that almost none of the patients had been advised by their physicians to have annual physical examinations. There were many patients who failed to report symptoms of pelvic cancer to their physicians, as well as an unfortunately large number of physicians who neglected to establish the diagnosis of pelvic cancer and to institute treatment. Delay in consulting a physician was found among 42% of the patients with carcinoma of the cervix, with an average delay period of 18 months. Delay in establishing a proper diagnosis was found among 19% of the physicians, and the average time elapsed between the patient's first visit to the physician and the establishment of the correct diagnosis was 9 months. Delay on the part of both patient and physician was found to be 14%, with an average delay period in consulting a physician and/or establishing a correct diagnosis of 14 months. Fifty-four per cent of the patients with invasive carcinoma of the cervic had no symptoms 6 to 12 months prior to consulting their physicians. Of the 46% who could have had their disease diagnosed before it became advanced, 16% delayed their visits to the physicians, and in 30% the physicians failed to make a proper diagnosis. Sixteen per cent of the patients with carcinoma of the endometrium delayed their visits to the physicians, and in 20% of these the physicians failed to make a correct diagnosis.

One cannot expect much improvement regarding delay in diagnosis and treatment until one impresses upon the public and the profession that in the majority of patients curable cancer is asymptomatic. The incidence of pelvic cancer can be materially reduced by physicians' stressing the importance of annual physical examinations and by the establishment of state and county committees for the study of pelvic cancer.

Cancer of the Cervix: Prevalence, Special Surgical Technique, and Evaluation of Results. S. Mitra. Cancer **11**:1190-1194 (Nov.-Dec.) 1958 [Philadelphia].

The anatomic distribution of cancer is not the same in different parts of the world. In a diagram the author shows the comparative incidence of cancer of different sites among patients in 2 institutions, the Cancer Hospital of Calcutta and the Royal Cancer Hospital of London. The preponderance of oral, laryngeal, and cervical cancer is marked in India. Cancer of the cervix constitutes 23.3% of all cancers in Indian women. This form of cancer was believed to be rare among Mohammedan women, but, in comparing the incidence of cervical cancer among Hindus and Mohammedans, the author found it to be practically the same. He believes that it is not the ethnological difference but the habits and the environment, the social status, and the assaults on the cervix from repeated childbirths that are responsible for the frequency of cancer of the cervix. There is no racial susceptibility to this type of cancer.

The author has been concerned with cancer of the cervix since 1924. During the early years of this period he treated all cervical cancers with irradiation therapy, as was then customary, but the first 5-year end-results were not encouraging, the cure rate being only 16.6%. Since then he has combined surgical with irradiation therapy. He resorted to Schauta's radical vaginal hysterectomy in preference to Wertheim's operation, because in India the primary mortality rate was much higher in Wertheim's than in Schauta's operation. There was only one ureteral fistula in a series of 391 patients operated on. Comparative 5-year end-results for patients with cervical cancer of stages 1 and 2 indicated better salvage with radical surgery (65.6%) than with irradiation therapy (43.5%). Postoperative complications were minimal with the author's technique of extraperitoneal lymphadenectomy and radical vaginal hysterectomy. Pelvic node metastases were found in 23.2% of the patients with cervical cancers in stages 1, 2, and 3 (38 of 164 in the newest series). The parametrium was rarely infiltrated; there was parametrial involvement in only 1 of 38 patients with metastases in the pelvic nodes.

The author concludes that the surgical method he employs in cervical cancer has definite advantages. This is substantiated by a 5-year salvage rate of 70% in patients with cervical cancers in stages 1, 2, and 3. Five-year survival has reached 84.6% for women in whom the pelvic nodes are not involved, compared with 43% for the group with metastatic cancer in the pelvic nodes.

***Twin Pregnancy in a Uterus Didelphys: A Case* Report.** W. M. Dawson and W. H. Ainslie. J. M. Soc. New Jersey **55**:649 (Dec.) 1958 [Trenton].

The authors present the history of a 22-year-old primigravida who was first seen on March 1, 1957. Her last menstrual period had been on Jan. 9, and her expected date of confinement was Oct. 16. Her antenatal course was uneventful until July 3, when palpation revealed the probable presence of a twin gestation and "double" uterus. There was a vertical midline groove on the uterus, giving an irregular "U" effect, with a distinct fetal heart in each limb of the "U." The patient went into labor spontaneously at 32 weeks of gestation. The first twin, a living male infant weighing 1417.5 Gm. (50 oz.), was delivered from the right uterus. The intact placenta was expressed spontaneously 5 minutes later.

At this time, the cervix of the left uterus was fully effaced and dilated to 4 cm., with bulging membranes which were ruptured artificially. Contractions continued irregularly and weakly in the left uterus. An infusion of oxytocin was begun with good results. and the second twin, a living male infant weighing 1615.9 Gm. (57 oz.), was delivered from the left uterus. The intact placenta was expressed 5 minutes later. Subsequent bleeding was minimal, and the patient's postpartum and puerperal course was uneventful. Both infants survived. The authors say that premature termination of pregnancy is usual in cases of double ovum twins, each twin residing in a separate half of a uterus didelphys, but the survival of such twins is extraordinary.

PEDIATRICS

Physiologic Abnormalities of Salicylate Intoxication. W. E. Segar and M. A. Holliday. New England J. Med. **259**:1191-1198 (Dec. 18) 1958 [Boston].

Forty-nine children were seen and treated for salicylate intoxication at the James Whitcomb Riley Hospital, Indianapolis, between 1952 and 1957. All were less than 6 years of age. Two were being treated for rheumatic fever. Of 43 with a history of salicylate ingestion, 11 children obtained the drug themselves or were fed it by an older sibling. The remaining 32 poisonings, primarily involving children under 2 years, were due to misguided therapeutic efforts of the parents, often upon the advice of a physician. There were 5 deaths, all in children less than 2 years of age; all 5 had severe hyperpyrexia. Eight children, of whom 6 were less than 2 years of age, had convulsions. The authors give particular attention to the metabolic alterations produced by salicylates. Hyperthermia, which is a prominent and occasionally a lethal result of salicylate intoxication, cannot develop unless the normal heat-regulating mechanisms are impaired. Since these mechanisms depend, in part, upon the evaporation of water from the skin and lungs, they are compromised by dehydration, which is observed in all children with serious salicylate intoxication. Both hyperventilation and sweating result in increased water and electrolyte expenditure. Vomiting and diarrhea occur frequently and contribute to the dehydration. Once the body water stores are depleted, salicylate can no longer induce effective sweating, and its hyperpyretic action is no longer balanced by effective defenses. Thus, hyperpyrexia accelerates dehydration, and dehydration potentiates hyperpyrexia. The greater loss of water than of electrolytes will result in hypernatremia.

Hyperglycemia occurred in 4 of the 14 children on whom appropriate studies were made. Salicylates have several separate pharmacological actions that alter carbohydrate metabolism. They increase "glucose demand," as well as the rate at which glucose is absorbed from the gastrointestinal tract; they probably increase the rate of production or of release of adrenal corticoids; and they interfere with the processes by which glucose is metabolized. Only the increase in glucose demand tends to lower blood sugar; the remaining 3 actions tend to produce hyperglycemia and glycosuria. The alterations in the carbohydrate metabolism also contribute to the production of ketosis. The urine of 30 children was examined for ketone bodies, and 27 of these tests were positive. Attention is called to the severe disturbances in the pH of the body fluids, including the early occurrence of a respiratory alkalosis, which is followed by a metabolic acidosis. The respiratory alkalosis is rarely of clinical importance except that it depletes the patient's buffering capacity and cation reserves for the acidosis that will follow. The various factors contributing to the metabolic acidosis, including abnormalities in carbohydrate metabolism and the production of ketosis, are reviewed.

Hyperthermia and dehydration are the immediate threats to life, and the initial therapy must be directed at their correction. External cooling with water or alcohol should be provided quickly to any child who has a rectal temperature over 104 F (40 C). Intravenous infusions of fluids must be prompt, because the patient's defense against hyperpyrexia can function only after the dehydration has been corrected. Electrolyte therapy, but not water, may be withheld until the presence of a metabolic acidosis can be confirmed and until the presence or absence of hypernatremia can be ascertained. Intravenous infusions of fluids similar to those that would be prescribed for a diabetic patient in acidosis should be planned for the succeeding 24-hour period. If the child is in shock or in impending shock, 20 to 30 ml. of Ringer's lactate solution per kilogram of body weight should be given rapidly before the 24-hour therapy is started. The initial fluids should contain no potassium. Other supportive measures may include the liberal parenteral administration of vitamin C and vitamin K.

A Controlled Study of Beta Hemolytic Streptococcal Infection in Rheumatic Families: I. Streptococcal Disease Among Healthy Siblings. J. M. Miller, S. L. Stancer and B. F. Massell. Am. J. Med. 25:825-844 (Dec.) 1958 [New York].

Data on the incidence of hemolytic streptococcic infections in 235 healthy children, between the ages of 5 and 16 years, who belonged to families that included at least one sibling with a definite history of rheumatic fever were collected from September, 1953, to June, 1956, at the House of the Good Samaritan, Children's Medical Center, Boston. Throat cultures and antistreptolysin O antibody levels served as the laboratory means of documenting all symptomatic streptococcic illnesses as well as asymptomatic streptococcic carrier states. Of 603 symptomatic respiratory illnesses occurring among the 235 children, 14% were associated with beta-hemolytic streptococci, and 90% of these organisms were of the group A variety. The most frequent clinical category of respiratory disease encountered was coryza which was rarely accompanied by laboratory evidence of streptococcic infection, whereas tonsillopharyngitis was the second most frequent clinical entity and showed a correlation with group A streptococci of 30%. Isolated fever was particularly associated with streptococci, and fever generally seemed to be the most important correlative finding of symptomatic streptococcic infection. Fully 55% of all group A hemolytic streptococcic infections observed were asymptomatic carrier states detected in children who were presumably well. Of the 603 symptomatic respiratory illnesses, 169 were group A hemolytic streptococcic infections. The diagnosis of group A hemolytic disease was made by positive culture in 157 (93%) of the 169, whereas immunological response alone was the basis for diagnosis in 12 (7%). Many different serologic types of group A organisms were detected among 151 isolations which were typed. Type 6 was most frequently encountered among the strains which could be typed. Of the 151 organisms studied, 53 (35%) could not be typed with the antiserums available. Suitable data on antistreptolysin O were available from 129 (76%) of the 169 group A hemolytic streptococcic infections observed, and a significant antibody rise was detected in 51 (40%) of the 129, of both symptomatic and asymptomatic groups of illnesses. The frequency of antibody response in the various categories of symptomatic streptococcic infection was about the same. Although the frequency of a significant antibody response seemed related to the numbers of streptococci in the throat, antibody rises occurred in the absence of positive throat culture in some cases. The 40% incidence of antibody response occurred in spite of early diagnosis and fairly prompt penicillin treatment of most such bacteriologically documented infections.

Three regimens of penicillin treatment were studied. An oral 10-day regimen of buffered penicillin G in a daily dose of 400,000 units was found to be suppressive for beta-hemolytic streptococci while the drug was administered, but bacteriological relapse occurred in 6 (30%) of 20 patients who received this treatment. A 10-day course of orally administered buffered penicillin G totalling 1.2 million units daily was highly effective in treating patients with symptomatic infections, was somewhat less effective in eradicating the carrier state, and was a failure in 9 (13.8%) of 65 patients so treated. A single intramuscular injection of 600,000 units of benzathine penicillin G failed in 4 (9.1%) of 44 patients. The oral program of treatment was well tolerated, with complete absence of side-effects of allergic reactions. The intramuscular preparation was tolerated with freedom from allergic reactions, but patients did complain of transient pain at the site of injection. Although no overt indication of typical rheumatic fever was seen after these 169 streptococcic infections, 2 instances of rheumatic heart disease appeared insidiously, and 1 instance of erythema marginatum was detected. The general occurrence rate of hemolytic streptococcic disease was greater among children of this study who still had their tonsils than among those whose tonsils had already been removed.

A Controlled Study of Beta Hemolytic Streptococcal Infection in Rheumatic Families: II. Penicillin Prophylaxis among Rheumatic Fever Subjects, Comparing Different Regimens. J. M. Miller, S. L. Stancer and B. F. Massell. Am. J. Med. 25:845-856 (Dec.) 1958 [New York].

The authors report on observations made during the period from 1953 to 1956 at the House of the Good Samaritan, Children's Medical Center, Boston, concerning the effectiveness of penicillin in the prevention of group A hemolytic streptococcic infections among children who were convalescing or who had completely recovered from acute rheumatic fever. A group of 452 hospitalized patients with acute rheumatic fever or a definite history of rheumatic fever received 200,000 units of buffered penicillin G given orally twice daily over the 3-year period. Another group of 114 rheumatic outpatients received 200,000 units of buffered penicillin G given orally twice daily, and 47 rheumatic outpatients received 1.2 million units of benzathine penicillin G intramuscularly at 4-week intervals. Healthy siblings of both outpatient groups of rheumatic children did not receive prophylactic penicillin and served as controls for measuring the incidence of streptococcic disease in these particular family environments.

No instances of recurrence of rheumatic fever developed among the entire group of 452 hospitalized patients, and in only 2 of these children did asymptomatic carrier states with group A streptococci develop. There was no case of elevation of antistreptolysin O among the entire group. There were 2 definite recurrences of rheumatic fever among the 114 rheumatic outpatients who received orally 200,000 units of buffered penicillin G twice daily, and there were no recurrences among the 47 rheumatic outpatients who were given 1.2 million units of benzathine penicillin G intramuscularly every 4 weeks. The oral regimen of prophylaxis achieved a striking reduction in streptococcic infections among the ambulatory outpatients receiving penicillin, as compared with their healthy siblings who were not so protected, and the intramuscular administration of long-acting penicillin showed even greater efficacy as a prophylactic agent. Among the 452 hospitalized rheumatic patients who received the continuous prophylactic amount of 200,000 units twice daily, there were only 3 with an untoward reaction of pruritic rash which required discontinuation of the penicillin preparation. None of the 114 outpatients showed adverse effects attributed to penicillin given orally. Subjective reactions among the patients who received penicillin intramuscularly were frequent. The reactions necessitated termination of this form of prophylaxis in 4 of these patients.

The results of this study have demonstrated the superior prophylactic benefit of repository injectable penicillin, but the risk of reactions has been greater than that associated with penicillin given orally. Oral therapy with penicillin is an effective agent in the prophylaxis of streptococcic disease, but continued cooperation by the patient is required in taking the drug by mouth. Both regimens have appropriate usefulness in the prevention of recurrences of rheumatic fever.

A Case of Cushing's Syndrome in an Infant. E. Goldblatt and A. H. Snaith. Arch. Dis. Childhood 33:540-542 (Dec.) 1958 [London].

The child presented was a girl, born after a normal pregnancy, who appeared normal when she was one year old. Two months later she was brought to hospital because of rapid gain in weight and increasing irritability. She was obese, with a buffalo hump, her face was plethoric, and she had an acneiform rash. There was slight hirsuties of the face and back. No striae were present. An intravenous pyelogram suggested enlargement of the right adrenal, and studies on the excretion of steroids revealed greatly increased values. In the expectation that an adrenal tumor would be found, an exploratory laparotomy was undertaken. Cortisone was given orally for 2 days prior to the operation. Both adrenals were found to be slightly enlarged and nodular. The left adrenal was removed, and after further investigation it was decided to remove the right adrenal. In preparation for the second adrenalectomy, cortisone was given orally and intramuscularly. The postoperative course was uneventful, the cortisone dosage was gradually reduced, and the patient was discharged 2 months later, by which time her appearance had become much more normal. At present she is on maintenance therapy with 20 mg. of cortisone acetate and 1 Gm. of salt a day. Three months after discharge the patient was again admitted to hospital, suffering from avulsion of 2 finger tips which had been caught in a train door. She withstood this trauma without any evidence of metabolic upset. The authors believe that this is the first time that adrenalectomy has been performed on an infant with adrenal cortical hyperfunction (Cushing's syndrome). The long-term prognosis remains to be seen.

Fourteen Personal Cases of Pneumocystis Carinii Pneumonia. G. Berdnikoff. Canad. M. A. J. 80:1-5 (Jan. 1) 1959 [Toronto].

The author reports on 7 male and 7 female infants with pneumonia due to Pneumocystis carinii, who were treated and who died at 4 hospitals in Canada between 1930 and 1958; the ages of the patients ranged from 2 to 4 months at the time of death. The clinical histories of the 3 most recent cases are summarized; these reflected rather faithfully the clinical aspect in all 14 patients whose lungs microscopically presented a typical picture of Pneumocystis pneumonia. Both sexes were equally affected. Four of the 14 infants were premature. Debility, whether due to prematurity or to other causes, seemed to be of major importance. The illness started with a sudden onset of periods of dry, unproductive cough accompanied by signs of suffocation. Cyanosis and polypnea were rather pronounced, and there was marked sternal retraction. Administration of oxygen usually brought relief, but symptoms recurred as soon as it was discontinued. There was no rise of temperature, except when the disease was complicated by another infection.

A symptom-free period of a few days' duration after the initial onset of the disease was definitely present in 7 of the 14 infants; it deserves special consideration, since it might become a valuable tool for the clinical diagnosis of the disease. The initial period of suffocation might be caused by edema and formation of hyaline pseudomembranes, which were well represented in certain regions of the lung of one of the patients, perhaps due to some hyperergic reaction. The disappearance of the exudate associated with pseudomembranes might then explain the remission of symptoms for a few days. This would be followed by new periods of suffocation, which now, however, were due to the direct obstruction of alveoli and bronchi by masses of the pullulating Pneumocystis organisms. Further observations are necessary in order to evaluate the exact incidence of the "symptom-free period."

Spontaneous pneumothorax was not rare among these patients. White blood cell counts varied between quite high values, up to 28,000 per cubic millimeter, and surprisingly low values, such as 8,900 per cubic millimeter, and for this reason cannot be depended on. The x-ray picture of the lung did not permit differentiation from other conditions, such as milk-aspiration pneumonia. There was absence of air usually in the perimediastinal regions of the lung parenchyma, accompanied by emphysema usually in the peripheral regions. The question of epidemiology still remains unanswered. Needle biopsy of the lung appears at present to be the only possible way of establishing a positive diagnosis during life. Nonfatal cases certainly exist, and it is left to the ability of clinicians to find a specific treatment.

Some Psychological Contributions to the Clinical Treatment of the Asthmatic Child. A. Macedo De Queiroz and A. Strauss. Acta allergol. 12:396-406 (no. 6) 1958 (In English) [Copenhagen].

The authors report on 40 children, between the ages of 2 and 11 years, with asthma who were admitted to the Hospital das Clínicas of the Medical School of the University of São Paulo, Brazil, and who were subjected to a specialized psychological study because of the close relationship between asthma and the personality of children. A clinical diagnosis of allergic asthma was the only factor in common of all the children in this group. They received medical treatment consisting of removal of specific allergenic factors and, when indicated, hyposensitization with allergenic extracts and autovaccines. Interviews were held with the patient and his relatives, and the patients were observed in free activities and were given psychological tests. The results of the psychological investigation revealed the existence of psychological factors directly related to asthma as causative agents, psychological factors indirectly related to asthma, and behavior problems frequently observed in children with asthma.

Direct influences included emotional tensions, resulting from conflicts at home, punishments, school examinations, parties, new situations such as entering school or playgrounds for the first time, and the feeling of being unwanted or having lost affection. The "use" of the asthmatic attack as a means to obtain specific ends, such as a mother's special care and attention, should also be considered as a factor directly influencing the disease. As indirect influences, there should be considered factors related to the emotional environment of the home, such as overanxious and depressive parents, marital conflicts, or unstable financial situations, and factors due to wrong educational attitudes, such as overprotection and constant vigilance over the asthmatic patient. Behavior problems accompanying the asthmatic symptoms included aggressiveness in 39 patients, anxiety in 32, overdependence on the mother or other family members in 28, anorexia in 23, fears in 23, negativism and stubbornness in 18, jealously, withdrawal tendencies, temper tantrums, and sleep disturbances in 13. These problems reflected clearly emotional and educational situations, as 34 of the 40 children had normal intelligence levels.

Combined psychological and medical-allergic treatment not only brought real benefit to the child's personality but also caused a more rapid improvement of asthma in all the children. Consequently psychological investigation seems absolutely justified. Psychopedagogic orientation to be given to the family is outlined. Psychological treatment, referring to the child's necessities and his psychological problems, was focused on enrichment of his experiences, canalization of aggressivity or elimination of its causes, elimination of causes of fear, support of achievements, and small tasks of responsibility at home. A specialized psychological examination would seem perfectly justifiable in patients with large psychological interference and when the family environment permits it.

Staphylococcic Pneumonia in Infants: Six Cases. E. Jaso and L. Abarca. Rev. españ. pediat. 14:663-676 (Sept.-Oct.) 1958 (In Spanish) [Saragossa, Spain].

Staphylococcic pneumonia is a severe and often fatal form of suppurative pneumonia which complicates some epidemics of influenza in infants. It is caused by Staphylococcus pyogenes var. aureus, which does not respond to treatment with sulfonamides, although it responds to chloramphenicol and to streptomycin. It may be complicated by (1) influenzal bronchitis, (2) a staphylococcic infection located at any distance from the respiratory tract, and (3) fibrosing pancreatitis. The early symptoms are those of pneumonia, with acute respiratory disorders: cough, dyspnea, fever, vomiting of hemorrhagic or purulent phlegm, and vascular shock. The roentgenograms of the chest are typical, showing innumerable pulmonary abscesses, both miliary and larger, up to 5 mm. in diameter. Most frequently the abscesses open into the pleura, causing empyema, pneumothorax, pyopneumothorax, or pneumatocele. Often there is a recurrence, with aggravation of the pneumonia.

Six cases of staphylococcic pneumonia in infants, between the ages of 1 month and 1 year, are reported. The predominant symptoms were typical of pneumonia in 4 cases and were similar to those of ileus in 1 and to those of pulmonary tuberculosis in 1. A diagnosis was made with certainty by the typical aspects of the lungs in roentgenograms of the chest, which showed unilateral pulmonary abscesses with pneumothorax or pneumatocele in 5 patients and bilateral pulmonary abscesses in 1. In all the patients there was polynuclear leukocytosis with intense nuclear deviation ("shift to the left"). Recovery was obtained through administration of erythromycin to 2 patients, of chloramphenicol to 2, and of streptomycin to 1. The patients with fibrosing pancreatitis and a pneumatocele died of recurrence of the pneumonia 4 months after the first attack.

Aminophylline Poisoning in Children. H. L. Bacal, K. Linegar, R. L. Denton and R. Gourdeau. Canad. M. A. J. 80:6-9 (Jan. 1) 1959 [Toronto].

The authors report on 10 children, between the ages of 8 months and 10 years, with aminophylline (theophylline ethylenediamine) poisoning arising from the therapeutic use of the drug in the management of bronchial asthma and upper respiratory infection. The drug was administered by the rectal route to 8 patients and intravenously to 1; in 1 patient the route of administration was not ascertained. The total known dosage ranged from 3¾ grains (225 mg.) for a 4½-year-old child to 22½ grains (1,350 mg.) in 36 hours for a 3½-year-old asthmatic child. Irritability, vomiting, hematemesis, and dehydration were nearly always present and complicated the preexisting disease for which the drug was administered. Albuminuria, drowsiness, convulsions, and cardiovascular syncope also were observed in some of the patients. Treatment of the intoxication was purely symptomatic, aimed at sedation, support of respiration and circulation, and prompt correction of dehydration. All the patients recovered and were discharged from the hospital within 24 hours to 14 days.

Theophylline is the most active of the xanthine agents, and the combination with ethylenediamine makes it more soluble and more completely absorbed. The xanthines stimulate the central nervous system, augment gastric secretions, cause diuresis, and exert central and peripheral actions on the cardiovascular system. The clinical manifestation of overdosage of aminophylline may be central nervous system stimulation with unusual restlessness and irritability; this is an early sign and may progress to tremors, epileptiform convulsions, drowsiness, and coma. Prolonged increase in gastric secretion may be manifested by nausea, persistent vomiting, or even hematemesis. Increased urine output may be associated with reversible albuminuria and dehydration. Cardiovascular collapse or even death may result. To eliminate preventable iatrogenic intoxication, the authors recommend the following dosages in the oral and rectal administration of aminophylline for the treatment of bronchial asthma in children: (1) suspension tablets given orally: 1½ grain (5 mg.) per kilogram of body weight; the dose may be repeated every 8 hours, but not oftener than every 6 hours; (2) rectal suppository or retention enema: ⅛ grain (7 mg.) per kilogram of body weight; the dose may be repeated every 8 hours, but not oftener than every 6 hours, and is to be restricted to patients in whom oral administration is not practicable. No undesirable side-effects were observed at the Montreal Children's Hospital with this regimen, which has been found adequate for treatment of children with asthma exclusive of those in status asthmaticus.

UROLOGY

Unilateral Multicystic Kidney: Report on One Case. G. Conca and E. De Nicolai. Minerva pediat. 10: 1097-1104 (Oct. 13) 1958 (In Italian) [Turin, Italy].

The authors report on a female infant with a unilateral multicystic kidney. At birth the child presented a mass which occupied the whole left flank; on the 5th day roentgenologic examination showed that the mass occupied the entire left side of the middle part of the abdomen and the uppermost part of the pelvis. The mass increased in size, and at the 8th month the child, who was otherwise in good condition, was operated on. A polycystic mass of the dimension of a small fetal head, occupying the whole left flank and part of the hypochondrium on the left, was isolated and enucleated. The mass substituted for the left kidney and showed some residue of parenchyma at the level of the hilus; the right kidney, the liver, and the pancreas showed no alteration. The mass was of a milk-white color and weighed 245 Gm. (9 oz.); its circumference was 21 cm. transversally and 26 cm. longitudinally. Structures identifiable as the vein and the artery of the kidney and a filamentous structure, a few centimeters long, without a lumen (probably an atresic ureter) were recognized. On section, the mass appeared to be composed of about 10 cystic formations of various dimensions and diameters. The cysts had a smooth surface and contained some clear watery liquid. The cystic cavities did not intercommunicate, and no excretory ducts were noticed macroscopically. Histological examination showed that the walls of the cysts were made up of connective tissue lined with cuboid epithelial cells. The tissue among the cystic cavities was made up of dense connective collagen. The child had a normal recovery, during which azotemia and urine tests gave normal values. Five months after the operation she was in good condition.

Evaluation of a Method for Detecting and Following Urinary Tract Infection in Females Without Catheterization. H. D. Riley Jr. J. Lab. & Clin. Med. 52:840-848 (Dec.) 1958 [St. Louis].

It is generally accepted that urine specimens for evaluation of urinary infection in women should be obtained by catheter, voided specimens being worthless because of contamination from the external genitalia. Yet there is evidence that bladder catheterization is not without danger of actually producing urinary tract infection. Patients immobilized by poliomyelitis and other paralytic diseases are particularly prone to infections of the urinary tract. A method of obtaining urine specimens for culture by a clean voiding technique without resort to catheterization was investigated in order to detect and follow the course of urinary infections in a group of paralyzed poliomyelitis patients. Subjects for this study included 34 female patients with paralytic poliomyelitis admitted to the Poliomyelitis Respiratory Center and 8 female patients with no clinical findings indicative of urinary tract infection admitted to other hospital divisions. Twenty-one of the poliomyelitis patients were over 15 years of age, and 13 were younger. Virtually all were immobilized and recumbent for long periods, and all except 2 experienced respiratory failure necessitating mechanical respiratory aids.

Urine for study was collected by the voiding technique. The first specimen passed by the patient in the morning was discarded. The second specimen was preferred. With the patient in the dorsal lithotomy position, the external genitalia were scrubbed thoroughly. Then the patient was encouraged to void, and the specimen was collected from the midportion of the urinary stream in a sterile container and immediately taken to the laboratory. It was either processed at once or stored in ice for not more than 3 hours. A catheterized specimen was obtained on the same day as the corresponding voided specimen, usually between 6 and 8 hours later.

Comparison of the paired samples collected from the poliomyelitis patients and from the controls according to the species and number of bacteria isolated revealed that satisfactory urine specimens for culture can be obtained by the voiding technique. When used in conjunction with colony counts or gram-stained smears of the urine, it is an adequate method of detecting significant bacteriuria in female patients. It is a valuable procedure for screening for urinary tract infection, especially in patients predisposed to urinary infection and in whom catheterization is almost certain to produce urinary infection. The risks inherent in bladder catheterization should not be neglected, and its use should be restricted to situations in which it is clearly indicated. To establish an accurate diagnosis of urinary tract infection, determination of the number of bacteria present in the urine is as important as their identification.

OTOLARYNGOLOGY

Carcinoma of the Larynx. G. E. Sheline and R. S. Stone. Ann. Otol. Rhin. & Laryng. 67:1066-1072 (Dec.) 1958 [St. Louis].

At a recent symposium on carcinoma of the larynx, sponsored by the American Cancer Society, it was evident that considerable disagreement exists in regard to the relative indications for surgery and radiation therapy. At the University of California Hospital in San Francisco a close cooperation has existed between members of the departments of otolaryngology and radiation therapy, which has resulted in a policy by which all carcinomas of the larynx are seen jointly by the staffs of the two departments. In general, radiation therapy was given preference in all cases in which there was a reasonable possibility that irradiation would control the lesion. The present review analyzes the results in 124 patients with histologically verified squamous-cell carcinoma arising in the endolaryngeal mucosa and treated by primary x-ray therapy during the period from July, 1942, through June, 1952.

Ninety-six of the patients had primary lesions of the vocal cord. Of these 96 lesions, 58 were controlled by radiation therapy alone; 2 radiation failures were controlled by secondary laryngectomy. Of the 30 patients with lesions which could have been treated by cordectomy, 24 received radiation therapy and were living and symptom-free at 5 years after treatment. Twenty nine of the 43 cord lesions which would have required total laryngectomy were controlled by irradiation alone. Five of the 19 patients with cord carcinoma, too advanced for control by laryngectomy, were salvaged by radiation therapy. Only 4 of the 26 supraglottic carcinomas were controlled by irradiation, but apparently none of the patients with these lesions would have been good candidates for surgery. Neither of the 2 subglottic carcinomas responded to irradiation.

Deafness Following Maternal Rubella: Results of a Prospective Investigation. A. D. M. Jackson and L. Fisch. Lancet 2:1241-1244 (Dec. 13) 1958 [London].

A national prospective inquiry into the effects of virus infections during pregnancy has recently been carried out by the Ministry of Health in Britain. During 1956-1957 a subsidiary investigation was undertaken on some of the children whose mothers had rubella during the first 18 weeks of pregnancy. The register of the national inquiry, which was compiled at the time of the mothers' pregnancy, included 79 surviving children from the counties of London and Middlesex whose mothers had rubella during the first 18 weeks of pregnancy. Fifty-seven of these children were still available for examination and constitute the rubella group. A control group, consisting of 57 children whose mothers had no infection during pregnancy, was also examined. The examination team consisted of a pediatrician, an otologist, an educational psychologist, and an audiology technician with experience in testing young children.

Reliable audiograms were obtained in all but 7 of the 114 children examined, and in these 7 the voice tests were considered adequate for the diagnosis of deafness to be confirmed or excluded. Fourteen of the 57 children whose mothers had had rubella during early gestation had congenital deafness. Such a diagnosis was made if the audiogram showed a hearing loss of 20 db. or more in at least 2 adjacent frequencies, or a loss of 30 db. or more in a single frequency. In 2 of the 7 children from whom reliable audiograms could not be obtained, a diagnosis of severe bilateral deafness was made on the results of other hearing tests. The remaining 5 children were considered to have normal hearing, but, in the absence of reliable audiograms, the possibility of minor degrees of hearing loss could not be excluded. In 5 of the 14 children the deafness was unilateral.

Since Gregg's original report on the effects of rubella during pregnancy in 1941, the early retrospective studies suggested that the incidence of congenital defect, including deafness, was very high. Later prospective investigations showed it as much lower. The authors believe that theirs is the first investigation to include detailed hearing tests with audiograms on a group of children from a prospective series. The group is to some extent selected, because it includes only live-born children from the national inquiry who survived to the age of 4 years and lived in the London area. The fact that 9 out of 14 cases of congenital deafness had not been detected by the age of 4 years indicates the importance of detailed hearing tests, including audiograms, in the diagnosis of deafness caused by rubella during gestation.

THERAPEUTICS

On the Use of Liver Extracts Regulating the Action of the Heart in Surgical Patients. C. Uggeri. Minerva med. 49:3928-3933 (Oct. 20) 1958 (In Italian) [Turin, Italy].

The author reports on his experience with Cortunon, an Italian proprietary liver-extract preparation which has a regulatory effect on the action of the heart. The extract was given to 174 surgical patients—to 83 before the operation and to 91 after the operation. The 83 patients who received the drug before the operation were given 3 intramuscular injections of 2 cc. per day for 2 to 4 days, followed by 2 injections per day, one in the morning and the other in the evening, for the remaining period preceding the operation, usually from 4 to 8 days. The treatment was resumed by mouth soon after the operation in half of these patients and was continued for a period of 5 to 10 days. Patients whose condition was serious received a beginning dose of 12 cc. per day, given in 3 injections, and a continuing dose of 6 to 8 cc. per day.

Liver-extract treatment in most of the patients was combined with analeptic or cardiotonic treatment and was well tolerated generally and locally. In 9 patients with exophthalmic goiter the drug was combined with other substances, such as iodine, sedatives, and vitamins. The heart condition of 6 of these patients improved within 2 to 4 days; their pulse rate diminished 20 to 35 beats per minute. In one patient the pulse rate which was 130 per minute was reduced to 80 per minute after 6 days of treatment with 6 cc. of Cortunon per day; the subjective symptoms disappeared. Three patients, who had been under medical treatment for several years but with poor results, derived no benefit from the liver-extract preparation until after a subtotal thyroidectomy. Poor results were obtained in 3 patients with essential hypertension, and there was no effect on the pulse rate of 4 patients with valvular lesions. Subjective symptoms, though, disappeared in 6 of 7 patients with coronary disease; in 1 patient with atrioventricular block and in 2 patients with early auricular fibrillation, the administration of Cortunon had a permanent beneficial effect.

Anticoagulants in Therapy of Arteriosclerosis. O. Castro Bianchino. Tórax 7:77-87 (March) 1958 (In Spanish) [Montevideo, Uruguay].

Eighty-three patients with arteriosclerosis were treated with anticoagulants during the past 3 years at the Puriel Semiologic Clinic in Montevideo. Before the treatment cholesterolemia was normal in 52 out of 66 patients and was increased in 14. The total lipids were normal in 35 out of 74 patients and were increased in 39. The lipidograms showed pathological tracings for 68 out of 83 patients and were normal for 15. The presence of hemorrhagic diseases and of diseases which are frequently complicated by hemorrhages was regarded as contraindication for anticoagulant treatment. Fourteen patients with myocardial or pulmonary infarction were treated with Tromexan (a coumarin derivative). The drug was given by mouth in an initial dosage which varied between 600 and 900 mg. divided into 2 or 3 fractional doses. The maintenance doses were regulated by the results of periodic determinations of the blood prothrombin time. Fourteen patients with cerebral or coronary arteriosclerosis or with arteriosclerosis of the legs had intravenous injections of a heparin solution, each injection containing 7,500 I. U. of the drug in 1.5 cc. The injections were given 3 times a week for 2 or 3 consecutive months. The remaining 55 patients were excluded from the study owing to their irregularity in reporting for consultation.

Either treatment was aimed at modifying the metabolism of lipids and the humoral changes which are responsible for pathological abnormalities in the wall of the arteries. Tromexan had no effect on the metabolism of lipids. Heparin, on the other hand, regulated the metabolism of *lipids* in the 14 patients to whom it was administered. The total lipids were increased in 10 patients, and the lipidogram tracings showed considerable improvement for 9. Great improvement from heparin treatment was obtained in 7 patients with anginal symptoms from coronary arteriosclerosis and in 4 patients with arteriopathy of the legs, with painful intermittent claudication. The satisfactory results have been maintained in all 11 patients for more than 3 months since discontinuation of the treatment. In the 3 patients with cerebral arteriosclerosis, though, the results of heparin treatment were mediocre. The tolerance of the 11 patients for heparin was perfect; none of them exhibited anaphylactic reactions. Since the treatment is expensive, it should be given only when (1) the lipidograms are characteristic of the disease, (2) there is a deficit in the amount of heparin in the blood, and (3) there are anginal symptoms or painful claudication of the legs.

Therapeutical Results as Obtained with Plasma Gamma Globulins of Human Origin: A Survey Covering 6,602 Cases: I. Main Indications for Their Use in Infectious Diseases. J. P. Soulier, M. Badillet and F. Herzog. Presse méd. 66:1881-1884 (Nov. 29) 1958 (In French) [Paris].

The authors give the results of a survey covering 6,602 cases of measles, whooping cough, rubella, mumps, smallpox vaccination complications, and smallpox, which were treated by the administration of plasma gamma globulins of human origin. The preparation was also used to prevent measles in 3,702 persons. The authors present results by groups in towns and in collectives. In the case of measles, injection of a solution of gamma globulins was generally practiced in the first half of the supposed incubation period of the disease. Complete protection against measles was provided for 878 persons out of 1,201 in the town group (73.2%). In 323 persons protection was not complete, and measles resulted, usually in an attenuated form; 125 of these patients had been exposed to prolonged contagion. In 3 of the failures titers of antibodies were insufficient, and in 19 of them the injection was given too late. Prophylaxis of measles in infants exposed to contagion was justified. The quality of attenuation was in direct proportion to the date of injection of the gamma globulin solution. In the group of collectives there were 3 categories: nurseries with healthy children; homes for children of different ages, frequently with physical weaknesses; and hospitals for sick children of different ages. A total of 2,501 children received injections; of this number 2,280 were completely protected against measles by the gamma globulin solution, but 182 had mild cases of the disease and 39 developed severe cases. Eighty-one patients who were given the preparation as a curative treatment of measles showed satisfactory results. In 12 patients measles was complicated by encephalitis, but 11 of them were completely cured.

Curative treatment of whooping cough with a solution of gamma globulins was beneficial for 150 patients treated at the Hospital for Sick Children in Paris. Therapeutic results were excellent in 144 patients, were average in 44, and were absent in 38. Preventive treatment of whooping cough resulted in complete protection of 360 persons out of 437 attempts. A survey of 349 patients was conducted essentially to define the preventive action of gamma globulin therapy on rubella in pregnant women and on congenital malformations in their children. Of 315 pregnant women, the majority of whom had been closely exposed to rubella, 312 were completely protected by the injection. The condition of the infant was described in 229 cases. Only one defect might possibly be attributed to rubella; this was a case of mental retardation, and it may not have been caused by the disease, because the exposure took place during the 6th month of pregnancy. Eight pregnant women with rubella received the gamma globulin solution curatively. The infant of one patient had not yet been born; the other pregnancies resulted in one miscarriage, one infant who died soon after birth, one infant with a light psychomotor retardation, and 4 normal children.

When the gamma globulin injections were used to prevent mumps, 92 out of 104 persons were completely protected, 10 contracted the mild form, and 2 developed severe cases. Thirty-six patients with mumps were treated with the preparation in an effort to shorten the course of the disease and to prevent complications. Results were good, particularly in orchitis parotidea which was cured in 3 or 4 days. Thirty-eight persons who had the gamma globulin treatment successfully escaped the complications of antismallpox vaccination. The therapeutic effect of these injections on 34 patients who developed such complications was good, with a rapid reduction in general signs and a fall in fever within a few hours. Sixty-eight persons who had been exposed to smallpox received the gamma globulin preparation, and all except 12 who had slight fever or benign smallpox escaped the disease. A cure with gamma globulin treatment was effected in one case of smallpox with complications.

Observations on Antibiotics in the Treatment of Hepatic Coma and on Factors Contributing to Prognosis. J. M. Stormont, J. E. Mackie and C. S. Davidson. New England J. Med. 259:1145-1150 (Dec. 11) 1958 [Boston].

The observation that urea-splitting bacteria in the colon were a significant factor in ammonia production and the demonstration of decreased portal-vein ammonia after the administration of antibiotics suggested that antibiotics should be of value in the treatment of hepatic coma. The combination of chlortetracycline with protein deprivation was shown to produce significant improvement in many patients with hepatic coma. Dietary protein has, however, been shown to be essential for adequate liver function in human subjects and animals. Neomycin administration to patients with chronic hepatic coma will allow additions of protein in amounts otherwise not tolerable. Since patients with cirrhosis may be in nitrogen balance with 30 to 50 Gm. of dietary protein, patients with hepatic coma at the Boston City Hospital have recently been treated with neomycin or paromomycin and protein withdrawal for 2 to 4 days; this was followed by administration of about 30 Gm. of dietary protein daily while antibiotics and other therapeutic measures were continued, the protein intake subsequently being increased as improvement occurred. In the last 2 years the authors studied 68 patients in hepatic coma or precoma. Sixty patients were considered to have cirrhosis of the alcoholic type, and 5 had "postnecrotic" cirrhosis, although a history of alcoholism was present in 2 of these. Two patients with hemochromatosis and one with metastatic carcinoma involving the liver were also included.

Seventy episodes of hepatic coma or impending coma were observed in the 68 patients, with recovery in 27 (39%). Twelve patients received chlortetracycline. Excluding these, there were 58 episodes in 56 patients, with recovery in 23 (40%) and improvement in 41 (71%), usually within 48 hours; of these 58 episodes, the patients in 34 were treated with paromomycin, resulting in 14 recoveries (41%), and in 24 with neomycin, resulting in 9 recoveries (38%). Thus, there was essentially no difference among the various antibiotics used in conjunction with readministration of protein. Comparison with 35 patients treated with complete protein withdrawal and chlortetracycline in the same hospital during the previous year also revealed no important difference in improvement and recovery. The majority of fatalities were related to potentially correctable complications, such as hemorrhage and infection. Liver failure was also an important cause of death, and prognosis was adversely affected by elevated serum bilirubin or electrolyte abnormalities. No evidence of neomycin or paromomycin toxicity was encountered, and severe diarrhea was not a problem with the doses used in this regimen.

Production of Impending Hepatic Coma by Chlorothiazide and Its Prevention by Antibiotics. J. E. Mackie, J. M. Stormont, R. M. Hollister and C. S. Davidson. New England J. Med. 259:1151-1156 (Dec. 11) 1958 [Boston].

Development of impending hepatic coma, characterized by confusion, drowsiness, and flapping tremor, has been described previously in patients with cirrhosis given nitrogenous substances by mouth—ammonium cation-exchange resins, ammonium salts, urea, methionine, and increments in dietary protein. It has also been reported in patients given a carbonic anhydrase inhibitor, acetazolamide. The authors here report the production of impending hepatic coma in alcoholic patients with cirrhosis and ascites given chlorothiazide, a nonmercurial diuretic agent. Chlorothiazide, administered to 5 alcoholic patients with cirrhosis and ascites, was observed to produce impending hepatic coma in 3 of these patients. This was associated with increased arterial ammonia concentration, increased sodium and potassium excretion, and a fall in serum potassium concentration. Impending hepatic coma was prevented by the concurrent administration of broad-spectrum, nonabsorbable antibiotics, and the oral administration of potassium chloride supplements prevented hypokalemia. The authors conclude that chlorothiazide is a useful diuretic agent in some patients with cirrhosis and ascites, but these patients must be carefully observed for the development of impending hepatic coma and hypokalemia. Potassium chloride supplements may be necessary.

PATHOLOGY

Malignant Cells in Peripheral Blood. J. C. Pruitt, A. W. Hillberg and R. F. Kaiser. New England J. Med. 259:1161-1164 (Dec. 11) 1958 [Boston].

This report is concerned with the study of results obtained by the use of a new method by which it is possible to examine quantitatively up to 20 ml. of peripheral blood for the presence of malignant tumor cells. In cooperation with the health office of Washington County, Maryland, and the private physicians of Hagerstown, Md., 20-ml. specimens of peripheral blood were obtained from a vein in the antecubital fossa of patients with and without cancer. The usual technique of venipuncture was used, but the syringe contained approximately 50 mg. of Lipo-Hepin to prevent coagulation. The blood was collected in sterile tubes and refrigerated for brief periods, permitting transport to the central laboratory.

The procedure for processing the blood was that described by Malmgren and associates (*J. Nat. Cancer Inst.* 20:1203, 1958). The procedure involves the addition of streptolysin O as hemolysin and leukocidin followed by passage of the resultant material through Millipore filters. Five or six filters are required for each specimen. The filters are removed after filtration from the special funnel apparatus and stained by the Papanicolaou technique. After staining, each entire filter is mounted on a glass slide and permanently sealed with permount and a cover slip. The slides are then ready for microscopic examination. Three hundred blood specimens, obtained from 100 patients with cancer and from 200 presumably well people, were studied. Examination revealed that cytologically malignant cells were identifiable in 39% of patients with cancer, and suspicious cells were present in an additional 12%. In the control group of 200 persons, cells that were considered to be cytologically malignant were found in only one (or 0.5%).

It seems likely that malignant squamous cells exfoliate into the blood at least as often as cells from adenocarcinomas. Sarcomas exfoliate cells into the blood with about the same regularity as carcinomas. Melanoma cells were found in the peripheral blood of 2 patients out of the 3 examined. These melanomas were not advanced, and the patient whose specimen was negative had been treated by total excisional biopsy 3 days before the specimen was obtained. It seems that one has about the same chance of identifying malignant cells in the peripheral blood in patients whose disease is local only but no treatment has yet been instituted as in patients whose disease has spread from its site of origin but treatment has been obtained. The reasons for this are not entirely clear, except that most often the spread of the lesion is to the lymph nodes, and these nodes may act as filters. A statistically significant analysis of the relation of the site of origin of the tumor to the presence of malignant cells in the peripheral blood proved impossible, but the biological activity of the tumor seems to be of importance. Malignant cells are not present in enough volume to justify examination of peripheral blood to make a primary diagnosis of cancer except in suspected cases that have eluded diagnosis by other means. Further evaluation of the method is required. It may be of value to follow patients after operation to indicate the presence of unsuspected metastases.

Analysis of Lipids of the Arterial Wall. C. J. F. Böttcher, J. G. Keppler, C. C. ter Haar Romeny-Wachter and others. Lancet 2:1207-1209 (Dec. 6) 1958 [London].

The authors carried out a detailed analysis of the lipids extracted from 22 single human aortas in different stages of atherosclerosis, which were obtained from autopsies performed at the laboratory of pathological anatomy of the University Hospital in Leiden, The Netherlands. Phospholipids, free fatty acids, sterol esters, glycerol esters, and free sterols were extracted from these aortas. The composition of the fatty acid mixtures from 4 of these 5 fractions were analyzed by gas chromatography. The results of these studies did not confirm the hypothesis that the deposition of saturated cholesterol esters is a characteristic feature of atherosclerosis. On the contrary, the proportion of saturated sterol esters fell as the severity of atherosclerosis increased, as also did the proportion of saturated phospholipids. The degree of saturation of triglycerides bore little relation to the degree of atherosclerosis. The authors decided to continue their analyses, paying special attention to the ratio between nonessential and essential unsaturated fatty acids deposited in the aorta, and a more detailed account will be published soon.

Experimental Production of Carcinoma with Tobacco Products: V. Carcinoma Induction in Mice with Cigar, Pipe, and All-Tobacco Cigarette Tar. A. B. Croninger, E. A. Graham and E. L. Wynder. Cancer Res. 18:1263-1271 (Dec.) 1958 [Chicago].

The authors previously published results of the experimental production of carcinoma of the skin in mice after application of cigarette tar condensate in 3 strains of mice, as well as in rabbits. The present study is concerned with comparing the biological activity of different types of tobacco products, such as cigars, pipes, and all-tobacco cigarettes. The smoking machine and the manner in which cigarettes were smoked and tars prepared for use were described in previous publications. A popular brand of cigars was puffed 3 times a minute, pulling a 50-ml. puff over a period of 4 seconds. This increase in volume and length of puff was necessary to keep the cigars lit and to give an adequate draw. The smoking time averaged 26 minutes. All-tobacco cigarettes were prepared by wrapping cigarette tobacco in tobacco leaf. These special cigarettes were smoked under the same conditions as standard cigarettes, but, owing to the waxy tobacco outer wrapping, they were smoked more slowly than the latter, averaging 16½ minutes per cigarette.

The most important finding of this study is that all types of tobacco smoke condensate tested have substantial carcinogenic activity. This observation is in line with human epidemiologic data which show a relationship between all types of tobacco smoke and cancer of the respiratory tract, that of cigarettes mainly for the lung and that of cigars and pipes primarily for the oral cavity. The highest percentage of both papillomas and cancers was found in the group of Swiss mice painted with nicotine-free pipe and cigar tars. This indicates a somewhat higher degree of carcinogenic activity for cigar and pipe tars than for cigarette tar and a somewhat less activity for all-tobacco cigarette tar compared with standard cigarette tar. Some of the differences could be a result of differences in biological variation. A comparison of whole tobacco tar with diluted tobacco tar suggests that dilution of tar accelerates tumor formation, apparently as a consequence of increased absorption of tobacco carcinogens. A comparison of the carcinogenic activity of freshly prepared tar with that of "old" cigarette tar showed no differences in activity. Present data reemphasize the viewpoint that tobacco carcinogens are formed during the process of combustion of tobacco and that the amount of tobacco carcinogens formed depends on the temperature reached and the completeness with which the combustion process occurs. Preventive measures directed toward reducing tobacco carcinogens must apply to all tobacco products.

Observations on Aberrant Renal Arteries Curving Around and Compressing the Renal Vein: Possible Relationship to Orthostatic Proteinuria and to Orthostatic Hypertension. H. Nathan. Circulation 18:1131-1134 (Dec.) 1958 [New York].

On the dissection of 400 renal pedicles obtained from 200 dissecting-room cadavers in Philadelphia and Jerusalem, the author found in 7 cases (3.5%) an aberrant inferior polar renal artery, curving around the normal renal vein. Six of these aberrant vessels were on the left side, and one on the right. The polar renal artery originated from the aorta below the level of the corresponding renal vein, and proceeded upward and laterally behind the vein. At the upper border of the vein, the artery curved downward and descended in front of the vein, to reach the kidney near its lower pole. The artery thus described an arch over the renal vein. In all instances the artery was intimately related to the renal vein, which appeared constricted and angulated under the arch of the artery. This kind of aberrant artery could be the cause of compression of the renal vein, particularly in the erect posture. The possible consequences of such compression are discussed with special reference to orthostatic proteinuria. The possibility also is considered of the aberrant artery being partially compressed by the renal vein, again particularly in the erect posture. Should this occur, an "intermittent Goldblatt mechanism" might be established, which would offer an explanation for the causation of some cases of orthostatic or postural hypertension described in the literature.

BIOCHEMISTRY

Critical Evaluation of the Precipitation Test for Systemic Lupus Erythematosus. L. E. Böttiger. J. Lab. & Clin. Med. 52:909-911 (Dec.) 1958 [St. Louis].

The precipitation test with which Böttiger is concerned was described by Jones and Thompson in The Journal, March 22, 1958, page 1424. The test is carried out by adding a 12% solution of *p*-toluenesulfonic acid in glacial acetic acid to serum. The authors claimed the test to be specific for systemic lupus erythematosus and stated that they had found very few false positives. These false-positive reactions were found in cases of hepatitis, in disseminated coccidioidomycosis, and in 2 cases of fulminating multiple myeloma. It is well known that an increase of the gamma globulin fraction in the serum is often found in systemic lupus erythematosus. This also is the case in diseases that give false-positive reaction. To test the hypothesis that the precipitation test is a nonspecific reaction, 158 serum samples were examined. All had been sent to the department of clinical biochemistry for various routine analyses from different departments of the Karolinska Hospital in Stockholm. Results of the examination of the 158 serums seemed to indicate that the test was not specific for systemic lupus erythematosus but dependent on the gamma globulin content of the serum.

Absorption of Vitamin B_{12} in Pernicious Anemia: Defective Absorption Induced by Prolonged Oral Treatment. M. Schwartz, P. Lous and E. Meulengracht. Lancet 2:1200-1204 (Dec. 6) 1958 [London].

The authors studied vitamin B_{12} absorption in patients with pernicious anemia, both treated and untreated. Without intrinsic factor the urinary excretion of radiocobalt (Co^{60}) vitamin B_{12} in 17 untreated patients with pernicious anemia varied between zero and 4.4% as compared with normal values varying between 10 and 40%. When Co^{60} vitamin B_{12} was administered together with 100 mg. of hog pyloric mucosa, the excretion in all the patients attained normal levels, with values ranging from 12.4 to 29.5%. All these patients with untreated pernicious anemia had some, although very slight, spontaneous intrinsic factor activity, the average excretion being 2.2% without supplementary intrinsic factor. Sixteen patients with pernicious anemia treated solely with new preparations of vitamin B_{12} combined with hog pyloric mucosa, administered orally for periods varying from 3 months to 4 years, were examined in the same manner without intrinsic factor and with 100 mg. of hog pyloric mucosa. Only 5 patients showed a normal absorption of vitamin B_{12}, and the remaining 11 showed blockage of absorption of vitamin B_{12}. Vitamin B_{12} absorption tests also were performed on 10 patients with pernicious anemia treated solely with the old-type preparations of crude stomach (pylorus) for several years. Of the 10 patients, 2 showed subnormal absorption values with 100 mg. of hog pyloric mucosa; but these patients, despite the extremely long period of therapy, absorbed vitamin B_{12} excellently, in sharp contrast to patients treated with combination preparations for quite brief periods. Most of the patients who have had pernicious anemia for a long time have lost the last spontaneous intrinsic factor activity, the average excretion of vitamin B_{12} without supplied intrinsic factor being 0.6%, as compared with 2.2% in the untreated patients.

The blockage of absorption of vitamin B_{12} caused by oral treatment of pernicious anemia with combined preparations of vitamin B_{12} and hog pyloric mucosa, demonstrated previously, was confirmed. Such blockage is very common, and it often occurs after treatment for a few months. Patients treated with preparations of crude pylorus either develop this blockage not at all or to a negligible extent. The blockage is related to hog pyloric mucosa. Vitamin B_{12} bound to this substance is poorly absorbed despite the presence of active human intrinsic factor. Alterations in the intestinal flora do not appear to explain the blockage. The blockage is not present in absorption tests with homologous intrinsic factor or with intrinsic factor from another species (rat). This observation supports significantly the hypothesis that blockage is an immunity phenomenon, the intrinsic factor being to some extent species-specific.

PUBLIC HEALTH

Effectiveness of Influenza Vaccines During an Epidemic of Asian Influenza. B. F. Gundelfinger, W. T. Stille and J. A. Bell. New England J. Med. 259:1005-1009 (Nov. 20) 1958 [Boston].

An epidemic of respiratory illness, associated with Asian influenza, occurred in the early fall of 1957 at the United States Naval Training Center, Great Lakes, Ill. Of 3,355 Navy recruits who arrived at Great Lakes between Aug. 7 and Sept. 18, 1957, about 30% were given a 1-cc. subcutaneous inoculation of monovalent influenza-virus vaccine (A/Japan/305-57) reported by the manufacturer to contain 200 chick-cell-agglutinating (CCA) units per cubic centimeter (vaccine A). Another group (about 30%) were given a 1-cc. subcutaneous inoculation of polyvalent influenza vaccine containing 250 CCA units, each of Formalin-inactivated A/Swine, A'/FM1, and B/GL/1739-54 viruses (vaccine B). The remainder of the recruits (about 40%) were given an inoculation of either a trivalent adenovirus vaccine or a placebo inoculation and served as controls. Of 964 recruits in whom febrile respiratory disease occurred during the study period from Aug. 25 to Nov. 9, 1957, 152 were inoculated with vaccine A, 299 received vaccine B, and 513 were in the control group. This gives an attack rate of 23.5 per 1,000 per week in the vaccine A group, 49.7 per 1,000 per week in the vaccine B group, and 58.9 per 1,000 per week in the control group. During the epidemic an 83 to 90% reduction in febrile respiratory illness was associated with prior inoculation with a monovalent Asian-influenza vaccine containing only 200 CCA units of A/Japan/305-57-strain virus. A similar 21 to 46% reduction was associated with prior inoculation with the polyvalent influenza vaccine not containing the Asian strain. Although a marked protective effect was noted as early as 10 days after inoculation, a slight beneficial result was noted before that time. No untoward reactions to the vaccine were observed. It is concluded that the Asian influenza vaccine was highly efficacious under the conditions of use at Great Lakes in the fall season of 1957.

Effect of Eradicating Brucellosis in Cattle on Incidence of Human Cases. J. R. Held, H. Bauer and R. L. West. Pub. Health. Rep. 73:1096-1100 (Dec.) 1958 [Washington, D. C.].

Brucellosis was first reported in humans in Minnesota in 1927, and there was a general trend toward an increasing number of cases until 1946. Since 1946 the trend has been downward, for whereas the case rate per 100,000 population was 13.84 in 1946, it was 1.94 in 1956. An awareness of the presence of brucellosis in the state was needed before the majority of cases could be diagnosed. In 1927 serologic and bacteriological services were introduced into the laboratories of the Minnesota Department of Health to aid in the diagnosis of brucellosis. These services have been used increasingly by practicing physicians since that time. The only cases counted by the Minnesota Department of Health are those confirmed by an agglutination test with a titer of at least 1:80, accompanied by clinical symptoms suggestive of brucellosis, or confirmed by isolation of the Brucella organisms from blood cultures.

This paper is particularly concerned with the effect of the area certification program on the number of human cases of brucellosis. In 1939 the Minnesota Legislature enacted a law authorizing the State Livestock Sanitary Board to control and eradicate brucellosis in cattle by means of an area plan. Under this plan all cattle owners in a specified area are required to participate in a testing program. The law also provides for the slaughter or isolation of all cattle reacting to tests and regulates the importation of any cattle into the area according to whether the animals, or herds from which they originate, are infected or not. By 1956 all the counties in the state were operating under this plan. Coincident with progress in the eradication of brucellosis in cattle, there has been a significant reduction in the number of human cases. Since 1940, when the first counties were certified, the case rate has been 3.12 times greater in noncertified than in certified counties.

Other factors undoubtedly affecting the number of human cases of brucellosis in Minnesota are the number of cattle in the state. From 1927 to 1948, when the number of cattle increased or decreased, there was a corresponding increase or decrease in the number of human cases of brucellosis. But from 1950 to 1956 the number of human cases declined markedly in spite of a high increase in the cattle population. This change in trend results from the elimination of some sources of human infection by the acceleration of the program of eradicating the disease in cattle.

BOOK REVIEWS

The ABO Blood Groups: Comprehensive Tables and Maps of World Distribution. By A. E. Mourant, M.A., D.Phil., D.M., Director, Medical Research Council Blood Group Reference Laboratory, Lister Institute of Preventive Medicine, London, Ada C. Kopeć, D.és Sc., Statistician, Nuffield Blood Group Centre, London, and Kazimiera Domaniewska-Sobczak, M.A., A.L.A., Librarian, Nuffield Blood Group Centre. Occasional publication no. 13 of Royal Anthropological Institute. Cloth. $8.50. Pp. 276, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada. 1958.

The authors of the monograph have made a useful contribution to physical anthropology by compiling and tabulating the results of the studies on the distribution of the A-B-O groups and the subgroups of A throughout the world. For all large populations, moreover, the frequencies of the blood group genes have been calculated and tabulated. A debt of gratitude is due the authors for having undertaken the Herculean task of culling the vast literature, classifying the data, computing gene frequencies, and publishing all this information in a single volume.

Recent Advances in Pædiatrics. Edited by Douglas Gairdner, M.A., D.M., F.R.C.P., Pædiatrician to Addenbrooke's Hospital, Cambridge. Second edition. Cloth. $9.50. Pp. 378, with 82 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England.

This edition follows its predecessor by four years with a compendium of 13 articles covering those pediatric fields in which it is considered that significant progress in understanding or treatment has recently been made. The contributing authors are English with the exception of three American writers of two chapters. The following subjects are covered: changes in circulation at birth and the effects of anoxia, hematology of infancy, jaundice in the newborn, physical growth, hypothyroidism, spina bifida cystica, hydrocephalus of infancy, the nephrotic syndrome, tuberculosis, rheumatic fever, the deaf child, and pyogenic osteitis. Each of these small monographs gives either a complete résumé of the present investigational or therapeutic understanding in its field or a survey of newer approaches made, as in the case of childhood deafness. The chapters on hematology, jaundice of the newborn, and rheumatic fever are the most extensive and are full of practical, useful information. The section on tuberculosis is informative as to the control of this disease and the influence of the newer drugs and hormones on its course. Some of the articles are based primarily on the author's experience while others quote extensively from the current literature. Every chapter has a good up-to-date bibliography. Thus each section provides an excellent orientation and survey of a field of pediatrics in which significant progress in treatment or knowledge has been made. The British concepts do not differ from those held in the United States. This book is recommended as a better than usual source of information on its 13 subjects for any physician concerned with these problems in children.

Streptomycin and Dihydrostreptomycin. By Louis Weinstein, Ph.D., M.D., Professor of Medicine, Tufts University School of Medicine, Boston, and N. Joel Ehrenkranz, M.D., Assistant Professor of Medicine, University of Miami School of Medicine, Coral Gables, Florida. Foreword by Chester S. Keefer, M.D. Antibiotics monographs no. 10. Under editorial direction of Henry Welch, Ph.D. and Félix Martí-Ibáñez, M.D. Cloth. $4. Pp. 116, with 13 illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22. Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

This book provides a clear and reasonably complete exposition of the history, properties, methods of susceptibility-testing and assay, bacterial resistance and synergism with other antimicrobials, pharmacology, untoward reactions, and uses in various types of clinical infections, including application in combination with other antibiotics, of streptomycin and dihydrostreptomycin. A brief final chapter describes the use of streptomycin in the isolation and culture of viruses. Although the authors have not attempted to review all previously reported studies, the book takes into account most of the important published papers on the streptomycins. It is unfortunate that no reference was made to the study reported by Wier and co-workers (*Dis. Chest* 30:628-632 [Dec.] 1956) which revealed that, from the standpoint of hearing impairment only, therapy with the combination of streptomycin-dihydrostreptomycin (Streptoduocin) may be more hazardous than with streptomycin alone. The bibliography provided is extensive and is annotated in the text. A subject index included at the end appears to be carefully compiled. This book should be welcomed by all clinicians as well as laboratory investigators who have a special interest in antibiotics.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

WEIGHT GAIN AFTER CESSATION OF SMOKING

To the Editor:—*Many persons who stop smoking quickly gain weight. In most of them this is undoubtedly due to an improved appetite with consequent increase in caloric consumption, but some who have "kicked the habit" stoutly maintain that they are gaining weight in spite of the fact that they have not increased either food or beverage consumption. Is there any metabolic change that might account for some of this weight gain?*

John Trapnell, M.D., Philadelphia.

Answer.—Weight gain after cessation of smoking, just as true weight gain under any circumstances, must be due to an excess of calorie intake over calorie expenditure. The insidious increase of calories is effected by two significant factors. Smoking may inhibit gastric motility for 15 to 60 minutes; consequently, in most chronic smokers hunger and appetite are depressed. Psychic restlessness, previously satisfied by smoking, is now appeased by the substitution of food. As in most obese persons, minor nibbling and between-meal snacks may add up to an astonishing number of calories. The pharmacological effects of nicotine are complex. An immediate stimulating action on the autonomic nervous system, the adrenal medulla, and vasomotor cortex occurs, which results in an increase in heart rate, cardiac output, and respiratory rate and elevation in blood pressure. These may, in turn, cause acceleration of metabolic processes, but this initial action is followed by depression of the same systems so that one must assume that the effect is the summation of these two phases. It must therefore be concluded that little alteration in metabolic processes occurs after cessation of smoking.

SKIN DIVING AND POLYCYTHEMIA VERA

To the Editor:—*Is there a relationship between skin diving and true polycythemia vera? In a 35-year-old man with a hemoglobin level of 21 Gm.%, should further diving be restricted?*

Richard O. Bagley, M.D., Richmond, Calif.

Answer.—Some distinction might be made between scuba diving (self-contained underwater breathing apparatus) and snorkel diving. The former does not involve breath-holding, but the latter does to some extent. Snorkel diving might therefore be expected to induce an adaptive polycythemia and intensify symptoms, if any, of an already existing polycythemia. This is purely theoretical, however, for no case has been reported of an adaptation of this sort or any deaths or sickness in skin divers with symptoms (thrombosis or hemorrhage) suggesting polycythemia as a contributory cause. There is no record of actual experience that would justify restricting this man's activities in this direction. A remarkable article by Auerback and associates (*Pediatrics* 21:54, 1958) includes mention of a 12-year-old boy who had hemoglobin levels as high as 24 Gm.% with no symptoms other than "pink-eye." These authors believed that the presence or absence of troublesome symptoms should determine whether anything should be done in the way of limiting activities or starting treatment.

MONGOLISM

To the Editor:—*An article in a Spanish medical journal discussed the treatment of Mongolism with androgens, with favorable results. Is dehydroepiandrosterone available in the United States? Please comment also on powdered calf pituitary extract in the treatment of Mongolism.*

O. L. Frank, M.D., Maquoketa, Iowa.

Answer.—Hormonal treatment of Mongolism was first advocated in the United States several years ago. The regimen advocated consisted of the oral administration of pituitary substance from the immature animal (calf), on the premise that the pituitary of the immature and adult animal differ in growth-stimulating ability, plus thyroid substance as a mordant. Several aspects of this treatment may be viewed with concern. The cause of Mongolism remains unknown. Although histological changes in the pituitaries and thyroids of affected persons have been demonstrated, there is as yet no evidence for hypofunction of these or any other endocrine systems in Mongolism per se. Several studies have shown normal thyroid function in patients with Mongolism. Bovine growth hormone has not proved effective in the treatment of growth failure in man. Animal studies have demonstrated no difference in the growth-stimulating ability of the immature and adult pituitary, and growth hormone is not effective by the oral route. Reports of this form of therapy have not shown significant improvement in Mongolism. Clin-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ical and biochemical evidence of hypothyroidism has been noted in some such persons and evidence of hyperthyroidism in a very few. Here, appropriate therapy may be directed toward the thyroid disturbance, but it leaves the Mongoloid state unchanged. There is no evidence of androgen deficiency in persons with Mongolism and, therefore, no rationale for its administration. There are no known indications for the clinical use of dehydroepiandrosterone. It is commercially available in the United States for laboratory use.

METHANE IN WATER SUPPLY

To THE EDITOR:—*A newly driven well, 380 ft. deep, emits what appears to be natural gas. Does this admixture of gas render the water hazardous for household use? Should the water be submitted for chemical analysis and, if so, to whom?*

Charles H. Kosmaler, M.D., Elmira, N. Y.

ANSWER.—If the gas is methane, as it probably is, the water is dangerous to use because of the explosion hazard. A method of collecting and analyzing water samples for methane is given by Buswell and Larson (*J. Am. Water Works A.* 29:1978, 1937). The state or local health department can give advice on this problem. Carbon dioxide is a more common gas in ground waters. Since carbon dioxide is removed by passage through lime water or sodium hydroxide, a qualitative test can be done to determine whether the gas in question is carbon dioxide.

CHRONIC OTITIS MEDIA

To THE EDITOR:—*A 15-year-old boy has had chronic otitis media for several years. The drainage is purulent and often sanguineous. Examination revealed an old perforation, now barely visible, with chronic inflammation and drainage over the canal and drum. Roentgenograms taken in July, 1957, and October, 1958, showed no change, no cholesteatoma, and apparently normal mastoids. Culture revealed Staphylococcus pyogenes var. aureus sensitive to chloramphenicol, streptomycin, nitrofurazone, neomycin, and erythromycin. Chloramphenicol by mouth and in ear drops was tried for one week with little change. Cortisone had been tried previously with transient success and later with no success. What treatment should be used?* *M.D., Washington.*

ANSWER.—This is a chronic suppurative otitis media. The information furnished is not sufficient for a specific answer. Regarding the roentgenograms, which were said to show no cholesteatoma and apparently normal mastoids, such films frequently do not give definitive information. Cholesteatoma in the attic, for example, may not show up on a roentgenogram except in special films which have been carefully made. The culture in a chronic condition is frequently not significant, since it varies from time to time. The most essential information needed to understand the pathological process in this case is the finding on otoscopic examination. For example, a perforation in the pars flaccida of the tympanic membrane or along the upper periphery of the drum has quite a different significance from a central perforation in the membrane proper. A history that includes such factors as recurring upper respiratory infections, allergic episodes, and obstruction to nasal breathing is significant. Without such information it is not possible to give an intelligent opinion as to how such a condition should be treated.

TRIPLE VACCINE

To THE EDITOR:—*Is triple vaccine (pertussis, tetanus, and diphtheria antigens) to be preferred to double vaccine (tetanus and diphtheria only) when immunizing children of grade school age?*

C. W. Truesdale, M.D., Glencoe, Minn.

ANSWER.—There should be no doubt that it is preferable to give the triple antigens rather than tetanus and diphtheria alone when conducting a campaign of primary immunizations. The pertussis vaccine might be omitted if a child was known to have had whooping cough. Pertussis can be a serious disease in young children as well as in infants.

COMPOSITION OF HYDROCELE FLUID

To THE EDITOR:—*Have any studies been made on the enzymatic activity (lipase, esterase, acetyl choline esterase, and blood amylase) of hydrocele fluid? Not infrequently, one sees calcific plaques in the hydrocele sac containing large amounts of cholesterol. Have any determinations of the cholesterol content of hydrocele fluid been made?* *Ralph R. Landes, M.D., Danville, Va.*

ANSWER.—Hydrocele fluid in infants and children is derived from the peritoneal cavity through a hernial sac. In adults, particularly in elderly men, such fluid may represent an exudate from neighboring structures and possibly be associated with some inflammatory processes. This may also be the case with encysted hydroceles in the neck of the scrotum along the route of the original peritoneal evagination. Available information on the chemical constituents of peritoneal fluid is adequate except for the possible presence of enzymes. Both peritoneal fluid and transudates contain about 95% water. Traces of other constituents usually are expressed in milligrams per 100 cc. of fluid. The average cholesterol content of transudates is lower (40 mg. per 100 cc.) than that of peritoneal fluid (60 mg. per 100 cc.), but there is a wide range of variability. Both concentrations are much lower than that of cholesterol in plasma (195 to 230 mg. per 100 cc.). Peritoneal fluid shows lower average concentrations in total nitrogen, albumin, and creatinine than do transudates. The pH of the two types of fluid is practically the same (7.4), as are the average content of chlorides, nonprotein nitrogen, urea nitrogen, and uric acid. Further details are given in the Handbook of Toxicology (edited by W. S. Spector, National Research Council, Philadelphia, W. B. Saunders Company, 1956).

OSCILLOSCOPE RADIATIONS

To the Editor:—*A patient has chronic erythema and edema of his eyelids and across the bridge of his nose. The findings are those of a contact dermatitis. The history reveals the use of an oscilloscope screen (5BP1-zinc orthosilicate) for observing electrical wave forms. The patient has spent as long as five hours at a time working with this instrument at a distance of about 14 in., although he states he averages only about one hour a week. Could this be the cause of his trouble?*

Edwin R. Ruskin, M.D., New Rochelle, N. Y.

Answer.—Although this query is lacking in much needed information, such as the wearing of spectacles, it is possible to state that any oscilloscope operating in good condition provides less threat of injury than equal exposure to a television screen. While some ultraviolet rays are generated, these are completely absorbed by the covering glass of the oscilloscope. The x-ray radiation is trivial in amount and soft in quality. Even at high relative acceleration potential the prospect of injury is less than that from the television screen. In the United States there are hundreds of scientists who for years, day in and out, have observed the oscilloscope screen without any record of injury at any time. It is stated that the observation distance is only 14 in. This, if true, might be conducive to more eye strain than in the case of a greater observation distance. Even so, eye strain would not account for the reported damage to the nose. Therefore, the condition described can have no connection to the power entering the oscilloscope or to any emanation therefrom.

CHRONIC ATROPHIC POLYCHONDRITIS

To the Editor:—*Is there a disease which has as one of its principal characteristics softening of the cartilages in the trachea and bronchi? This question concerns a patient whose larger bronchi and trachea tend to collapse on forceful inspiration and who is troubled with atelectasis.*

M.D., Minnesota.

Answer.—A rare disease, chronic atrophic polychondritis, is characterized by inflammatory destruction, degeneration, and fibrous replacement of cartilage throughout the body. It is likely to be prominent in the ears and in the cartilaginous portion of the nose. Some or all of the joints may be involved, as well as the costal cartilages, the larynx, and the entire tracheobronchial tree. The condition is often preceded by or associated with iritis or iridocyclitis. No infecting organisms have been found. Some patients respond well to treatment with steroids. While such a condition might be confined to the trachea and the large bronchi, such a case has not been reported. The nature of this condition is unknown, but it has been suggested that it is a peculiar form of allergic reaction. Chronic pulmonary disease with atelectasis, infection, and respiratory insufficiency has been the cause of death in the fatal cases.

RADIO TRANSMISSION THROUGH FILLINGS

To the Editor:—*A 32-year-old woman who has many silver fillings in her teeth, who is otherwise physically in good health, and whose only diagnosable disease is a chronic anxiety state claims that for many years she has been able to hear radio programs even when the radio is not turned on. This occurs from time to time, and if she turns on the local station she finds that what she has been hearing in her ears is the same program that is currently playing. She lives with her husband on a farm, and there is no neighbor's radio nearby. It has been said that occasionally silver fillings can do this sort of thing. Is this legend or fact?* *M.D., Ohio.*

Answer.—When certain metals and their oxides are in a strong signal field of a radio transmitter, rectification may occur with the reception of the signal without the usual receiving equipment. This has occurred from radiators, faucets, and electric stove heating units but never from amalgam restorations or fillings. It is assumed that the farm on which the patient lives is not near a powerful radio transmitter. If so, a more intensive study of this unusual complaint should be made to determine whether other members of the household hear these radio programs. If the programs are heard only by the patient, the diagnosis and treatment are obvious. In view of the known anxiety state of the patient, the chief complaint should be evaluated more critically.

TREATMENT OF POISONOUS SNAKE BITES

To the Editor:—*The comments on treatment of poisonous snake bite, which appeared in the Questions and Answers section of* The Journal, *Jan. 3, 1959, pages 164-165, give the impression of being the latest information with which all are in agreement. This is not true, however, and the reader should realize that they represent Mrs. Buckley's personal feelings. It is unfor-*

tunate that this has resulted in the manufacturer's deleting reference to incision and suction in the circular accompanying their antivenin. Much work has been done regarding the effects of snake venom on animals. This has led to various conclusions, many of which do not apply to man. Due to the very nature of the problem, there are no well-controlled series evaluating the various therapies. There is little doubt, however, that the emphasis is shifting from incision, suction, and application of the tourniquet to more liberal use of antivenin, but this does not mean that the older techniques are without value if sensibly applied. The use of an arterial occlusive tourniquet is contraindicated, but the use of a tourniquet to block lymphatics is indicated. Much of the venom is transported via the superficial lymphatics, and the envenomation does not become systemic until these communicate with the deep lymphatics at the axilla, popliteal area, thigh, or groin. These superficial lymphatics can be blocked with a tourniquet loose enough to permit adequate arterial and venous circulation. Incising fang marks only compounds local damage from the venom, but incising the advancing edema front plus suction does remove a significant amount of venom. This was demonstrated by Jackson 30 years ago (South. M. J. 22:605, *1929). One must be careful in evaluating the results of therapy because of the many variables in a snake bite. Mrs. Buckley's suggested treatment would be adequate for most copperhead bites but would be inadequate for the bite of a large Florida or western diamondback rattlesnake. Many copperhead bites may need only antivenin, but a serious rattler bite will need incision, suction, tourniquet, adequate antivenin, and vigorous supportive measures, such as administration of blood, oxygen, and corticosteroids.*

John W. Schmaus, M.D.
University of Kansas Medical Center
Kansas City 3, Mo.

To the Editor:—*My letter in* The Journal *of Jan. 3, 1959, on the subject of snake envenomation, is not merely an expression of personl opinion but a compilation of medical opinion, published and in process of publication, on which the new, officially approved direction circular is based. Nowhere have I stated that "all are in agreement." The direction circular states, "Use of a tourniquet, incision and suction was for centuries the only method available for management of envenomation; such measures are still used by some physicians. However, others are coming to the opinion that surgical intervention should not be necessary if serotherapy is adequate." Much work has been done with the effects of snake venom in animals. Contrasting the results of Dudley Jackson, all Parrish's envenomated dogs, that were treated with incision and suction only, died. Although lymphatic spread of the venom received in the bite does take place, according to published reports, it is now believed that this is not the whole story. Parrish, whose work is summarized in the direction circular, stated that if any significant amount of venom is to be removed locally, early rather wide excision is required. Miller pointed out that this would be impossible on the foot, ankle, anterior surface of the leg, hands, and forearms. Parrish also emphasizes that "wide excision of any suitable body area would, of course, entail subsequent plastic surgery."*

The armed services were concerned with the question of the most satisfactory method for treatment of envenomation, because of snakebite accidents to military personnel. The studies of Leopold and co-workers and the observations of other authorities culminated in the request by the armed services for a new antivenin package from which the suction device is eliminated. This new package has been developed and has been officially standardized for military use.

The recommendations for dosage as given in the new direction circular reflect the experience of a number of clinicians practicing in snake-infested areas, as follows:

"INITIAL DOSE. It is essential to inject a large enough initial dose to overwhelm the poison. The smaller the body of the patient, the larger the initial dose required. Because children have less resistance and less body fluid with which to dilute the poison, they may require twice the dosage of serum that suffices for adults.

"Inject the contents of 1 to 5 vials of Antivenin or more, depending on the size of the snake, the lapse of time between the bite and specific treatment, and the size and condition of the patient (severity and rapidity of development of symptoms). For bites by large rattlesnakes and large specimens of other crotaline species, especially the tropical varieties, at least 5 vials of Antivenin or more may be required. Seven to 10 vials have been administered as the initial dose in many cases. For adult patients, as those weighing 100 to 150 pounds or more, 1 vial may be sufficient to neutralize the venom from the less virulent species, especially those of moderate size; e. g., copperheads or pygmy rattlers. For a bite by a similar specimen in a 20 to 40 pound patient, 3 to 5 vials may be required. Envenomation by a large cottonmouth moccasin may necessitate use of as large an initial dose as that for bites by rattlesnakes.

"ADMINISTRATION. If the bite was inflicted on an extremity, inject part of the initial dose intramuscularly (into muscle) or subcutaneously (under the skin) at various points around the limb, above the level of the swelling. Inject the rest of the initial dose into a large muscle higher on the bitten limb (the outer side of the thigh, the buttock or upper arm). Do not inject the serum into a finger or toe" (Shannon).

"If the bite was inflicted on the head or trunk, inject the initial dose subcutaneously or intramuscularly about the edges of the swelling surrounding the wound. Antivenin also may be injected subcutaneously in the loose tissue of the abdominal wall or between the shoulder blades. If a large amount of venom has been introduced directly into a superficial vein, as in a bite on the face, it may be desirable to inject Antivenin intramuscularly or intravenously within a few minutes. For late-treated patients exhibiting systemic symptoms, and especially in grave cases, associated with coma or paralysis, large doses should be administered intravenously."

The reported experience of Ruggiero showed that adequate antivenin treatment was effective in a severe case of Crotalus horridus (timber rattler) envenomation. Under local measures the patient's condition deteriorated rapidly, and he was moribund when antivenin was administered but recovered rapidly when mechanical measures were discontinued and adequate serotherapy was applied.

Supportive measures are described in the direction circular, in part, as follows: "The patient's blood should be typed as early as possible, since hemolysins present in the venom soon alter protein structure, thus preventing accurate cross-matching" (Shannon). "ACTH and cortisone may be used as a supplement to specific treatment, to control urticaria and similar delayed manifestations of allergy to horse serum, antibiotics and the venom itself. Such agents, however, do not of themselves influence the outcome of snake poisoning" (Wood, Hoback, Green; Schöttler). "Doses of 25 mg. cortisone have been administered by mouth, beginning with the first injection of serum, and continuing every six hours until all symptoms of envenomation were under control and no further doses of serum were required." According to one observer (Hoback) "such treatment has aided in reducing morbidity and has prevented evidences of serum sensitivity, even in known serum-sensitive patients. In severe cases cortisone may be administered intramuscularly or by vein if necessary."

Laboratory and clinical evidence has shown that the new, improved antivenin, released in March, 1954, does neutralize the proteolytic enzymes as well as the other toxic factors present in crotaline venoms. It is quite true that neutralization of the venom with antivenin is the only measure (officially) recommended. Infiltration of antivenin around the site of the bite is not advised in the newly revised direction circular.

According to properly constituted authority, cryotherapy is interdicted as a form of treatment. The new, approved direction circular states that this method, "first advocated for envenomation by Crum in 1906, has no therapeutic value" (Shannon, Parrish, Wood, and numerous others) "and is to be avoided as a form of treatment." "Combination of ligature and crymotherapy was tried and discarded (Allen) because such measures failed to save the lives of experimentally envenomated animals" (Allen). "Chilling, by chemical or other means, produces no alteration in the toxicity of the venom," (Shannon, Wood). "Prolonged exposure to cold is liable to increase the damage (Shannon). Since cold arrests conduction in the sensory nerves, however, ice water has been applied temporarily, by compress, in an effort to reduce the pain until serum could be administered. After injection of an adequate initial dose of Antivenin, application of cold is unwarranted and should be discontinued."

I shall be happy to send copies of the new direction circular on request.

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BACTERIOPHAGE TREATMENT OF STAPHYLOCOCCIC INFECTIONS

To the Editor:—*In the Nov. 8, 1958, issue of* The Journal, *page 1423, is a question on bacteriophage treatment of localized or systemic staphylococcic infections. The answer states that "today there is no practical method of employing bacteriophage therapy in the treatment of staphylococcic infections." This statement requires additional elucidation. The therapy is little used and little understood, but it probably represents the approach of the future. In the Communicable Disease Section of the Los Angeles County General Hospital, cures of staphylococcic meningitis and overwhelming septicemia have been effected with freshly made preparations lysing the patients' organisms. The preparations were given intravenously in both cases as well as intrathecally in the case of meningitis.*

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To the Editor:—*In the Question and Answer Section of* The Journal, *Nov. 8, 1958, page 1423, the consultant says that the great hope that bacteriophages would serve as effective thera-*

peutic agents against staphylococcic infections has never been realized. However, there is evidence that, when Staphylococcus bacteriophages prepared specifically for therapeutic purposes are used, they are of value. Practically all Staphylococcus bacteriophages have little, if any, effectiveness in vivo because they are inactivated rapidly in the presence of whole blood, serum, and pus. Such bacteriophages usually are prepared against a single strain or a pool of staphylococci in nutrient broth or peptone-free broth, and in these highly artificial conditions they do possess demonstrable and consistent lytic power. In my experience, however, such bacteriophages are useless as therapeutic agents.

Staphylococcus bacteriophages that act effectively in whole blood, serum, and pus can be prepared. For therapeutic purposes only those bacteriophages should be used that are virulent for the offending strain of Staphylococcus in the presence of the specific patient's whole blood, serum, or purulent exudate. It is also important that the bacteriophage to be used therapeutically can bring about lysis or convert the strain from smooth to rough at a temperature similar to that of the patient from whom the organism was isolated. Staphylococcus bacteriophages that have these attributes and are administered correctly can be useful in the treatment of local or systemic staphylococcic infections.

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To the Editor:—*In* The Journal, *Nov. 8, 1958, page 1423, the reply about the presently accepted opinion of bacteriophage treatment of localized or systemic staphylococcic infections states that today there is no practical method of using bacteriophage therapy in such conditions. On April 1, 1958, the Lincoln Foundation, a nonprofit medical research organization with laboratories in Swarthmore, Pa., was granted U. S. Government License 299 for Bacterial Antigen–Staphylococcus Phage Lysates (Staphage Lysates-T. M.). New biological products today must pass rigid criteria and strict evaluations with evidence of the need and merits and safety before such license is issued. Administered by nasal aerosol, orally, and topically, Staphage Lysates provide a practical method of controlling staphylococcic infections which concentrates on an immunological and lytic approach to this increasingly serious problem. This super-vaccine with highly polyvalent phage activity enhances the natural, active defensive mechanisms of the host by lysing pathogenic staphylococci in their main habitat, the anterior nares. Staphage Lysates selectively kill Staphylococcus pyogenes var. aureus yet spare the useful saprophytes of the intestinal flora, so essential in the bacterial synthesis of vitamins. The lysates contain bacterial polysaccharides which have been shown to be a potent agent for stimulation of higher levels of serum properdin, providing a nonspecific immunity against invasion by all bacteria and viruses. Many of the older articles on bacteriophagy stressed the value of specific staphylococcic phages in the treatment of staphylococcic infections (Crutchfield and Stout,* Arch. Dermat. & Syph. *22:1010, 1930).*

I have contacted most of the competent authorities in the investigative field dealing with antibiotics. Laboratory studies with clinical evaluations are being conducted on many fronts, the results of which will be published soon. The emergence of resistant strains of Staph. pyogenes var. aureus shows that the probable answer to this perplexing problem may not lie in the development of more new antibiotics, or combinations of them, but in the host, his environment, and his protective mechanisms. Being a nonprofit group, the trustees of the Lincoln Foundation have not applied for a patent on their product, but they do wish to disseminate the more recent knowledge of staphylococcic phages gained in the past 12 years of intensive work with Staphage Lysates. We have profited immensely from the background of mistakes and truths obtained during the 1920's and 1930's when bacteriophage was in its heyday. These facts warrant a critical reappraisal of staphylococcic bacteriophagology in the fight to overcome the serologic supremacy of the pathogenic micrococci, especially since resistance to phagic lysis has not been observed and the "hot" epidemic, hospital strains of Staph. pyogenes var. aureus—phage pattern 80/81—are readily lysed by Staphage Lysates.

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MUSCLE CRAMPS

To the Editor:—*In* The Journal, *Dec. 20, 1958, page 2206, a question was asked relative to the treatment of muscle cramps. Years ago, a patient began having cramps in the legs at night and a colleague suggested the use of quinine sulfate, which he had given for years, with success. Since then, from personal experience and in patients, regardless of any rationale, it has worked, which seems to be sufficient justification for its use. One 0.3-Gm. capsule has usually been sufficient to ward off the attacks for weeks and often months. Failure has been extremely rare.*

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ORAL CHOLANGIOGRAPHY

A METHOD OF VISUALIZING THE "NONVISUALIZED" GALLBLADDER

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Lee Gillette, M.D., New York

Forty-six patients were selected for further study after routine cholecystography had failed to give satisfactory visualization of the gallbladder or bile ducts. When oral cholangiography was carried out in this group, there was visualization of the gallbladder or of the common bile duct with stones in 23 patients, visualization of the gallbladder without stones in 12, and no visualization in 11. Of these 11, 8 were operated on and were found to have obstructed cystic ducts. Three of these had acute cholecystitis, with gangrene in one. Nine patients were spared an operation when oral cholangiography demonstrated normal function and absence of stones in the gallbladder. Resort to oral cholangiography is therefore to be recommended when routine cholecystography fails to give decisive results, for it gives 65% additional visualization as compared to only 5 to 10% additional visualization with the double dose method.

THE PURPOSE of this investigation was to compare the results of oral cholangiography with those of intravenous cholangiography in revealing actual pathological conditions when routine oral cholecystography gave no visualization of the gallbladder, bile ducts, or stones. We herewith report the results obtained with our own technique of oral cholangiography. The procedure used is a modification of one previously described.[1] Forty-six patients are included in this report. Routine cholecystography had failed, in all cases, in visualization of the gallbladder. However, oral cholangiography did reveal shadows of the gallbladder, with or without stones, in 33 patients (65%).

Routine cholecystography results in nonvisualization of the gallbladder and bile ducts in about 10% of tests made. Routine repetition of the cholecystography, with a double dose of dye, gives additional information in only a small proportion of cases. In absence of jaundice or evidence of impaired liver function, nonvisualization of the gallbladder is presumptive evidence of pathological changes, usually with cystic duct obstruction. However, it

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Presented, in part, as an exhibit before the World Congress of Gastroenterology, Washington, D. C., May 25-30, 1958.

has long been known that these findings may not be evident at operation. Under these circumstances, cholecystectomy either fails to relieve the preoperative symptons or aggravates them in about half the cases.

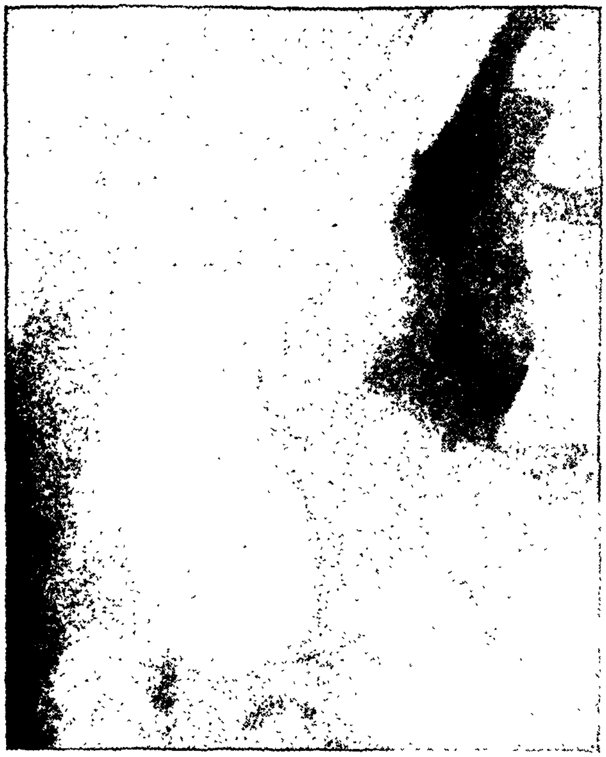

Fig. 1.—*Oral cholangiogram, showing normal visualization of the gallbladder without evidence of stones.*

Further information concerning the nonvisualized gallbladder may be obtained by intravenous or oral cholangiography. In the case of complete cystic duct obstruction ("physiological cholecystectomy"), both methods will fail to reveal a gallbladder shadow. As for partial obstruction of the cystic duct, most investigators have reported that iopanoic acid (Telepaque) is a more accurate indicator of disease because the intensity of the gallbladder shadow is dependent on its concentrating ability.[2] The triple dose of dye is used when a period of time has elapsed after the routine cholecystogram has been taken.

Instructions for patients with a previously nonvisualized gallbladder were as follows: On the evening before the roentgenograms were to be taken, the patient was given, at 7 p. m. (after 6 p. m. supper), 6 tablets of iopanoic acid with a glass of water. This was repeated a half hour later. At 9 p. m., 1 teaspoonful of paregoric in a glass of water was given. No fluids were to be taken during the night (other than specified). On the day the roentgenograms were to be taken, no breakfast wa allowed; at 7 a. m. the patient was given 6 tablet of iopanoic acid with a glass of water, and at 9 a. m the patient was given paregoric, 2 teaspoonfuls i one-fourth glass of water. The roentgenogram were taken at 10 a. m. and repeated at 11 a. m. an at noon. If no visualization of the *bile ducts* wa obtained, the films were repeated 24 hours later.

Results of Present Investigation

Forty-six patients are included in the report he presented. The patients were selected for study b the technique described because routine or cholecystography and, in some cases, intraveno cholangiography had shown inadequate or n visualization of the gallbladder or bile ducts. In n case was any specific diagnosis possible by previo roentgenographic tests.

For purposes of discussion, the patients a grouped on the basis of the results obtained wi oral cholangiography: (1) visualization of the ga bladder or of the common bile duct with ston 23 patients, (2) visualization of the gallbladd without stones, 12, and (3) no visualization of t gallbladder, 11 (in 6 of these the common duct w seen).

Stones were visualized in 23 patients in wh either gallbladder or common duct was seen. In t 18 patients of this group who were operated o roentgenographic findings were confirmed in cases. In 3 of the 18, there was visualization of t cystic duct up to the point of calculous ampul occlusion.

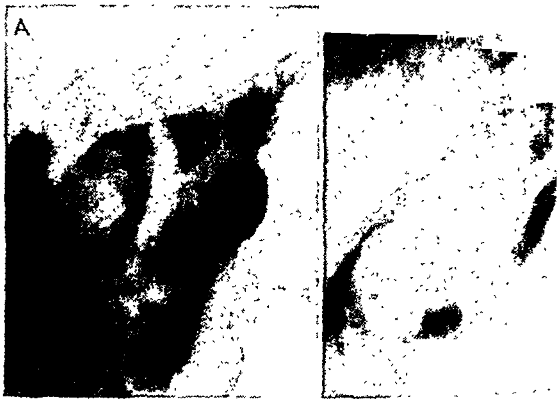

Fig. 2.—*Oral cholangiograms, showing, A, only comm duct and, B, common duct and cystic duct, with calcul ampullar obstruction.*

In the 12 patients with no stones and visuali tion of the gallbladder but not the common duct were operated on. Of these three, two had steno of the common duct sphincter without stones a one had acute cholecystitis. This patient had no stones in the gallbladder and one stone in the common duct. Thus, operation revealed common duct obstruction in each of the patients having no visualization of the common duct.

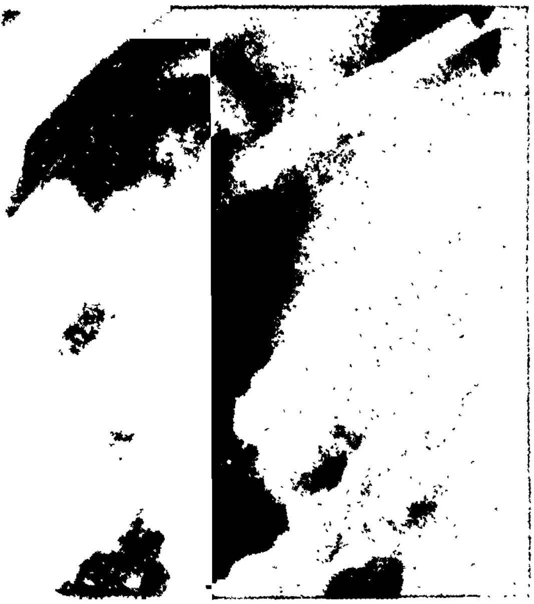

Fig. 3.—Oral cholangiogram, showing common duct and good visualization of gallbladder which contains multiple stones.

Of the 11 patients without visualization of the gallbladder, 8 were operated on. All had cystic duct obstruction. In six cases, the diagnosis was cholecystitis with cholelithiasis. In three of these, the condition was acute. Of these three patients, two had stones and one had gangrene of the gallbladder without stones.

Of these 11 patients, 6 had visualization of the common duct but not the gallbladder. Findings in the common duct were as follows: In three, the oral cholangiograms showed the common duct to be normal. In two of these three patients operated on for chronic cholecystitis with cholelithiasis, the common duct findings were confirmed. In the three patients in whom the oral cholangiograms showed dilated common ducts, the findings were confirmed at operation. In two of these patients the diagnosis of stones in the common duct, seen on the films, was confirmed at operation. In the third patient two small stones, found in the common duct at operation, were not seen in the films.

In summary, 33 patients had visualization of the gallbladder; an additional 6 had visualization of only the common duct. Twenty-seven patients were operated on. In 25 cases the diagnosis made by oral cholangiogram was confirmed at operation.

Diagnostic Use

Following is a discussion of findings in various conditions, including liver disease, catarrhal cholecystitis, pathological cystic ducts, chronic cholecystitis, and chronic cholecystitis with choledocholithiasis.

Disorders of the Liver.—As was previously noted, jaundice or impaired liver function will usually prevent visualization of the gallbladder by either the intravenous or the oral method. However, in certain patients without jaundice, oral cholangiography may clarify an otherwise obscure diagnosis.

Catarrhal Cholecystitis.—The group with catarrhal cholecystitis includes patients having relatively mild symptoms of gallbladder disease. In 25% of the patients of this series, oral cholangiography showed normal visualization and emptying of the gallbladder, without evidence of stones. This is illustrated in figure 1, an oral cholangiogram of a patient in whom, previously, a routine cholecystogram with a double dose of contrast medium had given no visualization. The patient was spared an operation.

Pathological Cystic Ducts.—Complete cystic duct obstruction will prevent visualization of the gallbladder by any method of cholangiography. However, oral cholangiography may reveal, under these circumstances, a common duct or, at times, visualization of the cystic duct up to the point of calculous obstruction (fig. 2). Patients of this series, with these cholangiographic findings, at operation showed hydrops of the gallbladder and acute or chronic cholecystitis, usually with cholelithiasis.

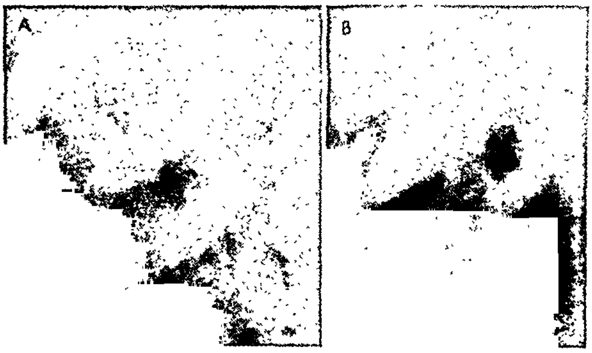

Fig. 4.—*A*, intravenous cholangiogram, showing only common bile duct (routine cholecystogram had twice shown no visualization). *B*, oral cholangiogram in same patient, showing common duct and faint visualization of gallbladder containing multiple negative shadows (operative findings included chronic cholecystitis with multiple stones and common duct normal, containing no stones).

Chronic Cholecystitis.—The greatest field of usefulness of oral cholangiography lies in furnishing definite diagnostic information in those patients with diseased gallbladder and partial cystic duct obstruction (fig. 3). Even in those patients in whom intravenous cholangiography has not given visualization of the gallbladder, oral cholangiography may be successful (fig. 4).

Chronic Cholecystitis with Choledocholithiasis.—Patients with diseased gallbladder and common duct stones may have visualization of neither the gallbladder nor the common duct, even with intravenous cholangiography. Due apparently to the longer period of dye excretion and concentration, oral cholangiography may reveal definite information under these conditions (fig. 5).

Combined Oral and Intravenous Cholangiography

In certain cases, where the use of oral cholangiography by the multiple dose technique results in no visualization or an unsatisfactory visualization, the addition of intravenously given iodipamide (Cholografin) may clarify the diagnosis. The injection may follow the third hourly oral cholangiogram or, preferably, be given after a period of 24 hours. After the dye is given intravenously, films are taken at 20-minute intervals for one hour or for two hours if the gallbladder is present. Figure 6 shows the results of such a procedure in a patient in whom the routine oral cholecystogram had shown no visualization.

Summary

A series of 46 patients, who on routine cholecystography had no visualization of the gallbladder or bile ducts, was studied with use of oral cholangiography. By this method, visualization of the gallbladder was obtained in 33 (65%). In 23 patients, oral cholangiography revealed stones not seen by means of oral cholecystography. Eighteen of these patients were operated on, and the diagnosis was confirmed in 17.

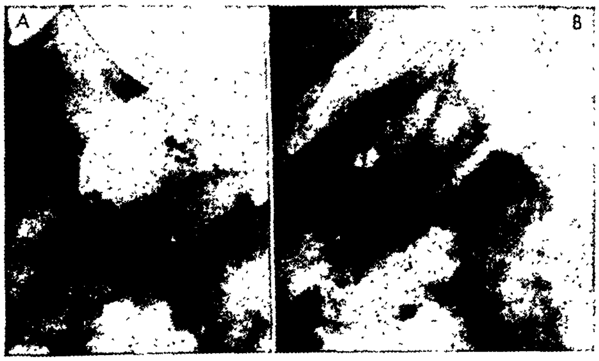

Fig. 5.—Oral cholangiograms, showing, *A*, gallbladder and dilated common duct, both with multiple stones and, *B*, faint visualization of gallbladder (*arrow*) and good visualization of common duct with choledocholithiasis (findings were confirmed at operation).

In 9 patients, oral cholangiography revealed normal gallbladder function and absence of stones. These patients were spared an unnecessary operation. These facts indicate that the gallbladder not visualized by routine cholecystography should be reexamined by oral cholangiography.

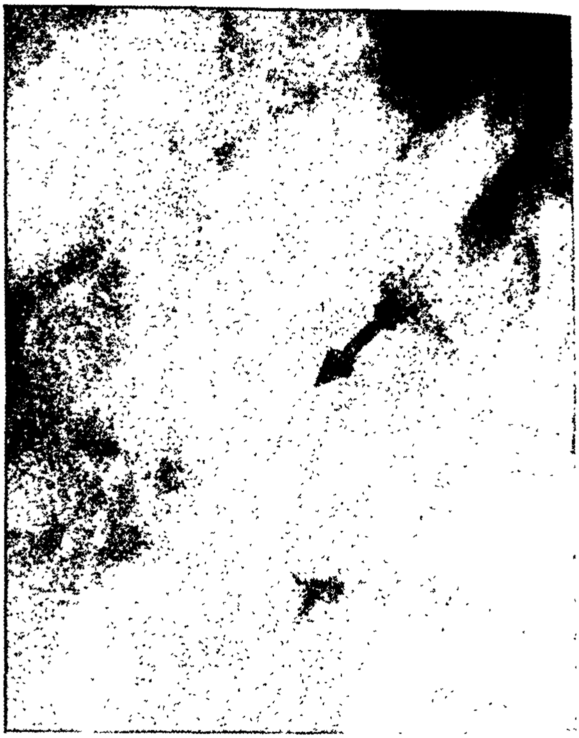

Fig. 6.—Combined oral and intravenous cholangiogram showing widely dilated common duct and gallbladder containing multiple stones. Oral cholangiogram had shown good visualization of the gallbladder and faint visualization of dilated common duct (*findings were confirmed at operation*).

850 Park Ave. (21) (Dr. Gillette).

This study was supported by grants from the Irwin Strasburger Memorial Medical Foundation and the R. Frankli Carter Foundation.

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SIMPLIFIED SCREENING TEST FOR CYSTIC FIBROSIS OF THE PANCREAS

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A test paper has been devised for use in quick examination of large numbers of people to detect increased concentrations of chloride in the sweat. The paper is impregnated with silver chromate, which is red. Upon contact with a solution of sodium chloride the red color is replaced by the white color of silver chloride. The paper was found easy to prepare, store, and apply, and after use it could be kept with the records of the case. Used in 91 healthy subjects and 9 patients known to have cystic fibrosis of the pancreas, it gave 3+ reactions with all the latter group. False-positive results were obtained in some children with fever or under emotional stress. Relatively strong (2+) reactions were obtained in some parents of children with cystic fibrosis, which is known to be inheritable.

Measurement of the chloride excreted by sweat glands in the hand has become a well-established diagnostic screening procedure for cystic fibrosis of the pancreas. It owes its inception to an astute clinical observation by Kessler and Andersen[1] during the New York City heat wave in August, 1948, that seven of the children hospitalized with heat prostration had cystic fibrosis of the pancreas. Elevated sweat chloride concentration in children, accompanied by relevant clinical data, is now usually considered strongly suggestive of cystic fibrosis and an indication for further diagnostic studies.

A simplification of the sweat test was reported by Shwachman and Gahm[2] in 1956. This method uses silver chromate in an agar base to assess the amount of chloride in hand sweat. As there is evaporation of water from the hand, the results are not a true indication of chloride concentration in hand sweat, but the test can be used for relative comparison between normal and diseased persons. This test has proved to be a most valuable screening procedure but it has some inherent disadvantages: The agar plates are bulky and must be refrigerated during storage; children tend to dig their fingers into the agar during testing; and the method provides no permanent record of the reaction.

A modification of this method was reported by Webb and Geiger[3] in 1957. The authors used a piece of filter paper on which a drop of 2% silver nitrate solution had been placed. The paper was grasped between thumb and forefinger by the test subject, and 10% potassium chromate solution was dropped on the filter paper. Increased sweat chloride levels were indicated by a light thumbprint on a dark background.

Simplified Test

These testing procedures have been further modified, and, we believe, simplified, by the impregnation of filter paper with silver chromate. In our tests we used no. 1 Whatman filter paper, 11 cm. in diameter. This diameter provides a complete hand print for most children.

The filter paper was dipped into 0.2 *N* silver nitrate solution, removed, blotted gently, and allowed to dry completely. The dried filter paper was then immersed in 0.2 *N* potassium chromate solution. It must enter this solution vertically so that both sides are exposed equally. Papers were then washed with distilled water to remove excess potassium chromate and immediately withdrawn and blotted. Prepared papers may be stored moist in an airtight container (we used plastic Petri dishes), or they may be dried and remoistened with water when ready for use. Papers must be kept in the dark; we have kept them for several months without any significant deterioration.

Testing Procedure and Results.—Fingerprints were made from the unwashed hands of test subjects and repeated at intervals up to 20 minutes after washing. For proper evaluation it was found necessary to wash the hands of the subjects; the best readings were made after a waiting period of 15 minutes. During this period it is desirable to protect the hand from contact with other parts of the body. For this purpose we used a fenestrated plastic football with an enlarged opening at one end. The child's hand was placed inside and the football secured in place by a gauze bandage.

Test papers must be moist when used. If stored dry, they should be remoistened with distilled water or tap water low in chloride content just prior to testing. They should be blotted gently before use, as prints are more distinct if the paper is not excessively wet. In testing, the patient's

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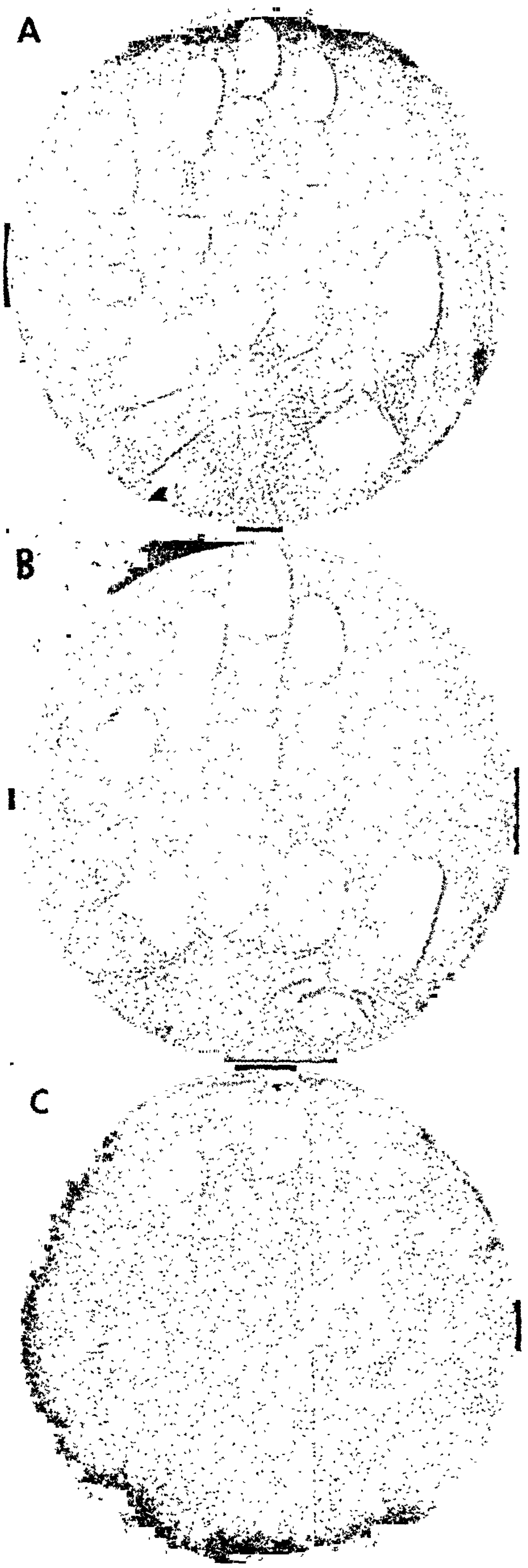
From the Department of Pathology, Hurley Hospital.



A and *B*, hand prints from children with cystic fibrosis of the pancreas, both graded 3+. *C*, test on normal child.

hand is pressed (with moderate pressure), pal down, onto the filter paper and held there f three or four seconds. In our experience it was n necessary to control precisely the length of tim that the hand is in contact with the filter pape as the available chloride is precipitated ve rapidly.

A result can be read immediately by compari the print to that of a normal control or to phot graphs of various prints. If the normal control pri is made at the time of the testing it must be membered that no relatives of patients should used as normal controls because of the heredita nature of the disease. Results are graded 1+, 2 and 3+ as suggested by Shwachman and Gahm False-positive results may occur in tests on febr children and those under considerable emotio stress.

Testing of 91 normal children and adults a 9 persons with known cases of cystic fibrosis vealed results similar to those obtained by t agar plate method (see figure). Reactions in p tients with cystic fibrosis all fall in the gro arbitrarily classified as 3+. All of these patie gave relatively heavier prints with the volar s faces of the proximal and middle phalanges the full hand print was taken, relatively hea ridges in the print of the palm were also observe Indistinctness of the print due to heavy blotchi was also characteristic of certain of the tested p tients with cystic fibrosis. Relatively strong (2+) actions have been encountered in some parents patients with known cases of cystic fibrosis. Af testing, the silver chromate-coated papers w dried at room temperature in a dark location. Th remained stable and provided a lasting record the reaction.

Summary

The impregnation of filter paper with sil chromate provides an improved method of scre ing children for cystic fibrosis of the pancreas. is similar to the agar plate test now widely us but has the added advantages of being less pensive to prepare and much easier to store, a it provides a lasting record of the reaction.

This study was aided by a grant from the Ames Comp Inc., Elkhart, Ind.

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RELATION OF FIBROSIS OF THE PANCREAS TO FATTY LIVER AND/OR CIRRHOSIS

AN ANALYSIS OF ONE THOUSAND CONSECUTIVE AUTOPSIES

Edward E. Woldman, M.D., David Fishman, M.D.
and
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For the past 35 years, the association of pancreatic disease and fatty infiltration of the liver with subsequent fibrosis has been observed frequently. Allan and associates[1] have shown that depancreatized dogs developed marked fatty infiltration of the liver even while they were maintained on therapy with an adequate amount of insulin. Montgomery and associates[2] were able to produce fatty changes in the liver of dogs after ligation of the pancreatic ducts.

It has been demonstrated by Dragstedt and associates[3] that feeding these animals raw pancreas prevented the development of fatty livers. Hershey and Soskin[4] have shown that the oral administration of lecithin has the same effect, and Best and Huntsman[5] have proved that choline, a derivative of lecithin, is also effective in preventing the development of fatty livers in experimental animals.

Later studies revealed that fatty livers were due to a deficiency of choline and other lipotropic substances resulting from the incomplete digestion and absorption of dietary protein in the absence of proteolytic enzymes of the external secretions of the pancreas.[6]

This experimental work on animals stimulated the interest in the development of fatty livers and cirrhosis in patients with diffuse pancreatic disease. Case reports began appearing in the literature dealing with fatty livers in patients with pancreatic disease. These included 2 cases of pancreatic lithiasis and atrophy reported by Snell and Comfort,[7] 2 of pancreatic fibrosis and atrophy by Cole and Howe,[8] and 10 of carcinoma of the pancreas involving the ducts and producing obstruction with secondary atrophy by Schnedorf and Orr.[9] All these cases were associated with fatty liver.

In the more recent reports, there were larger groups of patients with diffuse pancreatic disease with associated fatty livers. Edmondson and coworkers[10] found fatty liver in 17 (65%) of 26 patients with pancreatic lithiasis and chronic pancreatitis. Sanes and co-workers[11] found fatty changes and/or cirrhosis in all seven cases of pancreatic lithiasis. These studies were made on data from postmortem examinations.

The possibility that fibrosis of the pancreas might be related in some way to disease of the liver was explored in a study of material from 1,000 consecutive autopsies. Among these, 778 were free from disease of the liver; in the remaining 222 there was either fatty infiltration or cirrhosis or both. Fibrosis of the pancreas was present in 234 cases and absent in 766. There were 156 cases in which fibrosis of the pancreas was present together with involvement of the liver. This indicates a high degree of association between the two conditions.

There seems to be sufficient evidence both experimentally and in postmortem material to indicate that disturbances in pancreatic function may lead to fatty changes in the liver with subsequent fibrosis. In the early stages, the liver is fatty and the fatty change is important in the development of the later diffuse fibrosis. The next is the fibrofatty stage, and the advanced stage is the fibrotic stage. The present study is a report on 234 cases of pancreatic fibrosis and its relation to fatty liver and/or cirrhosis.

Material and Method

Our material was drawn from 1,000 consecutive autopsies at St. Luke's Hospital, Cleveland. The microscopic sections of the pancreas and liver were carefully reviewed by one of us (A. J. S.), and only those showing fibrosis of the pancreas were chosen for study. We did not include any case of acute pancreatitis, as we know that it takes several weeks or months of pancreatic insufficiency to produce a fatty liver. Fibrosis of the pancreas leading to pancreatic insufficiency is the end-result of severe or repeated damage to this gland. This condition is usually diagnosed at surgery or at postmortem examination and rarely diagnosed clinically.

We grouped the cases of fibrosis of the pancreas into three groups, those with fatty liver, those with fatty liver and cirrhosis, and those with cirrhosis. The first group was graded as mild, moderate, or severe, according to the degree of fatty change in

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the liver, and the second and third groups were graded as mild, moderate, or severe according to the degree of fibrosis.

Results

Fibrosis of the pancreas was observed in 234 (23.4%) of the 1,000 consecutive autopsies examined in our series. It occurred most frenquently during the fifth and sixth decades of life and was uncommon in the first two decades of life. The sex distribution was 131 males and 103 females (table 1). Of these 234 cases of pancreatic fibrosis, only 31 (13%) were with diabetes mellitus.

TABLE 1.—*Age and Sex Distribution of 234 Patients with Pancreatic Fibrosis*

Age Group, Yr.	Male, No.	Female, No.	Total
20-29	1	2	3
30-39	8	5	13
40-49	11	12	23
50-59	39	25	64
60-69	41	38	79
70-79	21	15	36
80+	10	6	16
Total	131	103	234

Fibrosis of the pancreas occurs in two major groups of patients, those with biliary tract disease and those who are chronic alcoholics. Among the 234 patients in our series there were 87 (37%) with associated disease of the biliary tract, such as cholelithiasis or cholecystitis. We were unable to obtain the exact data on the incidence of alcoholism in our series of fibrosis of the pancreas, as most of the cases were diagnosed during postmortem examination. Although a history of alcoholism was present in many cases, the data were insufficient for statistical purposes.

Of the 234 patients with fibrosis of the pancreas in our series, 156 (66.6%) showed either fatty liver alone or fatty liver and/or cirrhosis. There were 117 showing fatty liver alone, 32 showing fatty liver and cirrhosis, and 7 showing cirrhosis alone, or a total of 156 patients showing liver involvement (table 2). Among the entire group of 1,000 consecutive autopsies, there were 150 with fatty liver and 72 with fatty liver and/or cirrhosis, or a total of 222 patients with liver involvement. Of this total, 156 (70.3%) also showed pancreatic fibrosis.

Comment

A great deal of emphasis has been placed on the nutritional factors in the etiology of fatty liver and/or cirrhosis. The best evidence that nutritional factors are involved in the pathogenesis of fatty liver and cirrhosis comes from a consideration of kwashiorkor, which commonly occurs in tropical areas.[12] The diets of populations of the areas in which this syndrome occurs are low in protein, especially that of animal origin. In patients with kwashiorkor, in addition to changes in the liver, there have also been pathological findings of atrophy of enzyme-secreting cells of the pancreas, which may represent the primary lesion of kwashiorkor and may be responsible for the changes in the liver. We do not know the precise cause of the atrophy of these cells in the pancreas.

The association of alcoholism with fatty liver and cirrhosis was observed for many years and is now generally accepted. It has been observed by Patek and Post[13] that the conditions of patients with liver cirrhosis and a history of alcoholism improved when they received an adequate diet without cutting down on alcohol intake. The concept of cirrhosis in the alcoholic has been reoriented toward the nutritional aspects. There is no doubt that chronic alcoholics reduce their food intake to undernutritional levels. However, evidence of cirrhosis of the liver may occur in alcoholics who appear well nourished or, in fact, obese and may not be apparent in undernourished alcoholics.

Higginson and co-workers,[14] from their studies with such underprivileged Africans as the Bantu, doubt whether nutritional factors alone can be held responsible for the frequency of liver disease. Undernourished people in prison camps during World War II rarely showed evidence of liver involvement. A human diet deficient in lipotropic factors is hard to imagine and must be rare. Pancreatic insufficiency must be an important factor in causing a deficiency in lipotropic substances with the development of fatty liver and/or cirrhosis.

In most cases of alcoholism, as in kwashiorkor, pancreatic disease plays an important role in the development of fatty liver and cirrhosis. There is a rather high incidence of alcoholism in most reported series of acute and chronic pancreatitis.[15] Edmondson and co-workers[10] reported that 58.8% of their group of patients had a history of alcoholism, and Comfort has reported an incidence of 68%. There are other factors besides alcoholism which may be responsible for pancreatic disease, such as biliary tract disease. However, Owens and Howard[16] reported that 32 patients, who were diagnosed at Grady Memorial Hospital as having pancreatic calcification, were all chronic alcoholics.

TABLE 2.—*Incidence of Fatty Liver and/or Cirrhosis in 234 Cases of Fibrosis of the Pancreas*

	Mild, No.	Moderate, No.	Severe, No.	Total
Fatty liver	46	61	10	117
Fatty liver and cirrhosis	5	14	13	32
Cirrhosis	0	2	5	7
Total				156(66.6%)

Every patient was studied for evidence of gallstones by cholecystography, laparotomy, or autopsy and none were found.

McGowan and co-workers [17] have shown that hydrochloric acid and alcohol, when passing into the duodenum (after oral ingestion of alcohol), causes a spasm of the sphincter of Oddi. After large quantities of alcohol are taken orally, edema of the duodenal mucosa and papilla of Vater may also occur. This edema had been noticed in alcoholics at autopsy. From the results of experimental studies of Dreiling and co-workers [15] and from the investigative work of others, we can say that the role of alcohol in the production of pancreatitis is neither by the direct stimulatory effect on the pancreas nor through toxic action. Rather, it is suggested that the oral intake of alcohol causes the pancreas to secrete a large volume of pancreatic juice against an obstruction to the flow of secretion (spasm or edema). Rupture of the finer radicles of the pancreatic tree may result from the sudden increase in the intraductal pressure. Chronic pancreatitis is the end-result of many such episodes. Dreiling and associates [15] also found that when alcohol was administered intravenously in man to a point of intoxication it did not have any effect on the pancreas.

Clark [18] reported 44 cases of pancreatitis occurring in patients with acute and chronic alcoholism from autopsies at Bellevue Hospital, New York. In 24 the liver was large and fatty, and in 17 cirrhosis was present.

Pancreatic fibrosis results in pancreatic insufficiency due to the atrophy of the enzyme-secreting cells. The absence of the proteolytic enzymes of the external secretions of the pancreas causes incomplete digestion of dietary protein resulting in a deficiency of choline and other lipotropic substances. A deficiency of choline results in a deficiency of phospholipid synthesis and a failure of fat transport or oxidation, and, as a consequence, fat accumulates in the liver, leading to fatty liver with subsequent cirrhosis.

The so-called alcoholic cirrhosis or nutritional cirrhosis is not the result of a deficiency in dietary protein, as is frequently found in chronic alcoholics, but is, rather, the result of pancreatic insufficiency (due to disease of the pancreas) plus a low intake of dietary protein.

Summary

There is a definite relationship between fibrosis of the pancreas with pancreatic insufficiency and the development of fatty liver and/or cirrhosis. Reports in the literature have emphasized the fact that chronic alcoholism plays an important role in the etiology of fibrosis of the pancreas. The so-called alcoholic cirrhosis or nutritional cirrhosis is not the result of a deficiency in the dietary protein but is, rather, the result of pancreatic insufficiency plus a low intake of dietary protein.

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BACTEREMIA DURING PARTURITION

PREVENTION OF SUBACUTE BACTERIAL ENDOCARDITIS

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Blood samples for bacteriological study were obtained from 101 obstetrical patients immediately after delivery of the placenta, and again on the morning of the first postpartum day, in order to observe the frequency of bacteremia during labor. Four of the samples at the end of labor yielded bacterial growth, one organism being a coagulase-positive staphylococcus. Eleven of the samples obtained next day yielded growth, one organism being an alpha-hemolytic streptococcus. Thus, only two potentially pathogenic organisms were found, but the hazard of bacteremia in connection with labor was seen to be real. Patients believed to be susceptible to recurrent subacute bacterial endocarditis appear to need the same protection during parturition as is needed by similar patients during dental extractions, tonsillectomies, and urologic procedures. Prophylaxis with antibiotics is therefore justified in such cases.

Recognition of the transient bacteremia which frequently follows various operative procedures has resulted in successful prophylaxis against subacute bacterial endocarditis. The use of antibiotics in conjunction with dental extractions, tonsillectomies, and urologic procedures in patients with valvular or congenital heart disease is supported by careful bacteriological studies. Despite the occasional occurrence of subacute bacterial endocarditis after parturition, the hazard of bacteremia during normal labor has received no adequate documentation, to our knowledge. As a result, although most authorities endorse the prophylactic use of antibiotics in patients susceptible to bacterial endocarditis,[1] others omit this recommendation.[2] Therefore, it seemed appropriate to determine the incidence of bacteremia in normal labor and to review the pertinent clinical experience.

Materials and Methods

Specimens of blood were obtained in 101 consecutive patients immediately after delivery of the placenta, omitting only those patients with a history of recent antibiotic therapy for obstetric or medical reasons. Follow-up cultures were obtained in each case on the morning of the first postpartum day. The antecubital veins were used for withdrawal of blood after preparation with iodine and alcohol. Five cubic centimeters of blood was placed in Bacto-tryptose broth and 3 cc. was placed in thioglycollate broth. The cultures were examined for growth at the end of approximately one week. At the end of two weeks, in all instances, smears were made and transfers to blood agar plates were done. Incubation was aerobic and anaerobic, and the plates were kept for 48 hours before being discarded as negative.

Bacto-mannitol salt agar was utilized as a selective medium for the isolation of pathogenic staphylococci. The coagulase test was done on colonies having yellow zones. The ability to grow in a 6.5% sodium chloride solution was used to differentiate enterococci.

Results

Of the 202 samples taken from 101 patients, growth was obtained in 15, 4 in samples at the end of labor and 11 from blood obtained on the first postpartum day. In no patient did both samples on consecutive days reveal growth. Fourteen cultures yielded Staphylococcus (Micrococcus) species, most of these only in the thioglycollate broth. Only one was coagulase positive. A single alpha-hemolytic streptococcus was isolated in a postpartum specimen. This failed to grow in 6.5% sodium chloride solution and thus was not an enterococcus.

The patient with alpha-hemolytic streptococcus bacteremia proved to have been included in our study inadvertently. She had inactive rheumatic heart disease and had taken a sulfonamide daily prior to labor. Through oversight, she was given no antibiotic coverage during parturition. Six subsequent blood cultures were negative, however, and no clinical evidence of bacterial endocarditis appeared during the next two months.

The charts of the remaining 14 patients with positive cultures were reviewed. Only three had transient fever in the postpartum period. One had endometritis caused by a beta-hemolytic streptococcus, another had Escherichia coli pyelonephritis, and in the third the temperature elevation for one day was unexplained.

The percentage of staphylococcus isolations was no greater than that encountered in our laboratory

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as contaminants in routine blood cultures. This interpretation is supported by the fact that all but one were coagulase negative. The single alpha-hemolytic streptococcus and the coagulase-positive staphylococcus were the only organisms which may be considered potentially pathogenic, especially the former because of its frequent isolation in instances of subacute bacterial endocarditis.

Comment

The rarity of bacteremia after parturition in this study does not invalidate the recommendation that prophylaxis against bacterial endocarditis be used in susceptible patients. Our data indicate the minimum rather than the maximum possible incidence of postpartum bacteremia. An important bacteremia may be extremely transient, as was demonstrated in studies after dental extraction by Okell and Elliott.[3] We deliberately obtained initial cultures at a time when placental sinusoids are maximally dilated; nevertheless, more frequent cultures might have yielded a larger number of positive results. However, in an unpublished study by Ramsey and Swartwout,[4] 74 blood cultures obtained in 17 patients during and at various intervals after labor were uniformly negative.

Despite its low incidence, the seriousness of bacterial endocarditis warrants the use of prophylactic therapy in patients with predisposing heart disease. Of Wheeler's 200 cases of subacute bacterial endocarditis, 9 were precipitated by abortion or delivery.[5] In the extensive British experience reported by Cates and Christie,[6] the three postpartum cases of endocarditis were each caused by alpha-hemolytic streptococci. One case followed abortion; in this an enterococcus was isolated. In Geraci and Martin's study[7] of 33 cases of enterococcic endocarditis, one resulted from normal delivery, another followed dilation and curettage, and three more followed abortion. A questionnaire survey and review of the literature by Pedowitz and Hellman[1d] revealed 120 cases of bacterial endocarditis associated with pregnancy; 85 of these patients had been treated prior to conception, and 35 cases were incurred during pregnancy. Pregnancy itself was not associated with an unusual risk of relapse, though parturition was implicated in the recurrence of bacterial endocarditis in three patients. From the data given we cannot determine whether these recurrences represented new infections or were relapses of smoldering disease. However, it is significant that all three occurred among the 18 patients given no prophylactic antibiotics immediately before, during, or after labor. Among 102 patients receiving some prophylactic therapy, no recurrences or new cases of bacterial endocarditis were identified.

The choice of antibiotic regimens remains open. The tetracycline drugs apparently sterilize the parturient uterus far more effectively than does penicillin.[8] On the other hand, the objective of prophylaxis is prevention of bacteremia rather than reduction of uterine bacterial flora per se. For this purpose the bacteriocidal action of penicillin should prove advantageous. Since treatment of established enterococcic endocarditis usually requires streptomycin as well as large doses of penicillin, it might be reasonable to include the former in the prophylactic regimen. In any case, therapy should probably be initiated at the onset of labor and continued through the third postpartum day, as is recommended in other procedures associated with a hazard of bacteremia, and maximal antibiotic levels should be achieved shortly after delivery is completed.

Summary

From 202 blood samples obtained immediately after the third stage of labor and on the first postpartum day in 101 patients, only two potential pathogens, an alpha-hemolytic streptococcus and a coagulase-positive staphylococcus (micrococcus) were cultured. Postpartum bacteremia is probably an infrequent occurrence. The two positive results obtained and the accumulated clinical experience, however, amply justify the prophylactic use of antibiotics to prevent subacute bacterial endocarditis in susceptible patients during and immediately after labor.

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ASSOCIATION OF SPECIFIC OVERT BEHAVIOR PATTERN WITH BLOOD AND CARDIOVASCULAR FINDINGS

BLOOD CHOLESTEROL LEVEL, BLOOD CLOTTING TIME, INCIDENCE OF ARCUS SENILIS, AND CLINICAL CORONARY ARTERY DISEASE

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Three groups of men, selected solely according to the behavior pattern which they habitually manifested in their work, were compared with respect to their serum cholesterol levels, clotting times, presence of clinical coronary disease, and presence of arcus senilis. A group (A) of 83 men were chosen as manifesting an intense, sustained drive for achievement and as being continually involved in competition and deadlines, both at work and in their avocations. In this group the serum cholesterol level, the frequency of arcus senilis, and the incidence of coronary artery disease were much higher than in a group (B) of 83 men who manifested the opposite sort of behavior pattern and a group (C) of 46 unemployed blind men selected as manifesting a chronic state of insecurity and anxiety. Clinical coronary artery disease was seven times more frequent in group A than in group B or group C. Analysis of factors other than the overt behavior pattern described indicated that this pattern per se was largely responsible for the striking differences found.

We previously reported results of a survey in 209 lay executives and physicians of their opinion of major causes of clinical coronary heart disease.[1] The majority of both groups believed that a person's chronic exposure to emotional trauma resulting from excessive "drive," competition, meeting "deadlines," and economic frustration was the major cause.

Acting on this possible lead, we studied serum cholesterol levels and blood clotting times of owner accountants before, after, and during isolated intervals of exposure to environmental influences that induced this emotional trauma.[1] Accountants were selected because their daily business life is relatively free of chronic lack of time, competition, and the need for intensive drive, except for isolated intervals. The results indicated that, independent of changes in diet or physical activity, their exposure to a situation capable of provoking an emotional complex induced a marked rise in serum cholesterol level and acceleration of blood coagulation.

Therefore, we considered it important also to study people who were more or less continuously immersed in the same emotional complex that only occasionally involved the accountants. Such a group had to be selected with care and compared with a second group not similarly exposed. Moreover, it was considered advisable to investigate a third group of persons who were not exposed to the above specific type of emotional activities but who displayed obvious evidence of a different type of emotional disturbance, namely, chronic anxiety. The results are reported here.

Methods of Study

Formulation of Behavior Patterns.—In order to study the possible pathogenic propensities of a particular emotional complex, formulation was made of a specific overt behavior pattern (pattern A) that we believed either was associated with or actually induced abnormal changes in serum cholesterol level and blood clotting time. Our belief stemmed from the above studies as well as from our own clinical experiences with younger patients suffering from clinical coronary disease.

This overt behavior pattern was characterized as follows: (1) an intense, sustained drive to achieve self-selected but usually poorly defined goals, (2) profound inclination and eagerness to compete, (3) persistent desire for recognition and advancement, (4) continuous involvement in multiple and diverse functions constantly subject to time restrictions (deadlines), (5) habitual propensity to accelerate the rate of execution of many physical and mental functions, and (6) extraordinary mental and physical alertness.

A second overt behavior pattern (pattern B) then was formulated. Essentially the converse of pattern A, it was characterized by relative absence of drive, ambition, sense of urgency, desire to compete, or involvement in deadlines.

A third overt behavior pattern (pattern C) also was formulated, characterized by its similarity to pattern B but also including a chronic state of anxiety or insecurity.

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Read, in part, before the Annual Meeting and 31st Scientific Sessions of the American Heart Association, San Francisco, Oct. 26, 1958.

Selection of Three Study Groups.—In the selection of group A (overt behavior pattern A), the aid of certain laymen of various corporations, independent companies, and newspaper organizations was requested. The behavior pattern and the general nature of the study were explained, and they selected associates most closely fitting this pattern, regardless of position, health, or other factors. It was hoped that a relatively random group of people might thus be chosen exclusively on the basis of their adjudged overt behavior pattern. Moreover, such persons were selectees rather than volunteers. Over 96% of the men selected subsequently agreed to cooperate.

The subjects were selected from engineering, paper manufacturing, and aluminum corporations, newspaper organizations, advertising agencies, grocery chains, television stations, and other independent businesses. Since selection was made on the exhibition of a particular behavior pattern and not because of economic position, various types of executives and nonexecutives were included in this group. Thus, it should be stressed that this is a study concerned not with the position but with the overt behavior pattern of the subjects.

Eighty-three men comprised group A. Eighteen were aged 30-40 years; 43 were aged 40-50 years; and 22 were aged 50-60 years.

Since we intended the men in group B (overt behavior pattern B) to be closely similar to those in group A in relevant physical and physiological respects, and differing essentially only in their overt behavior pattern, they were not selected until the group A men had been interviewed. Again, various businessmen and labor union officials selected for us the men of this group. They were selected from an employees' union of a municipal government, a union of professional embalmers, and 12 accounting firms. The members of these latter firms, unlike those of our earlier study,[1] did not have proprietor or partner status and were studied in February, a month relatively free of occupational urgency for accountants.

Group B also consisted of 83 men. Twenty-nine were 30-40 years of age; 37 were between 40 and 50; and 17 were between 50 and 60.

The primary reason men of group C (overt behavior pattern C) exhibited little ambition, drive, or desire to compete was the presence of total blindness for 10 or more years and the lack of occupational deadlines because none was gainfully employed. Their behavior pattern differed from that of subjects in group B only in their exhibition of a chronic state of insecurity and anxiety, due not only to financial insecurity but to the constant hazards to their physical security incurred in daily living.

Forty-six unemployed blind men were selected for us. Twenty-one lived in an institution, and 25 lived in their own homes. Sixteen were 30-40 years of age; 13 were between 40 and 50; and 17 were between 50 and 60.

The Personal Interview.—Each of the 212 subjects was carefully interviewed concerning parental incidence of coronary artery disease, past and present illnesses, hours of work and sleep, smoking habits, physical activity of all types, and dietary habits.

Then the degree of development of his particular behavior pattern was assessed by one of us prior to any subsequent procedures. The men of groups A and B were subdivided depending on whether they appeared to exhibit a completely or only an incompletely developed overt behavior pattern. Thus, a person was adjudged as exhibiting completely developed behavior pattern A if he exhibited various signs we believed indicative of its presence, including excessively rapid body movements, tense facial and body musculature, explosive conversational intonations, hand or teeth clenching, excessive unconscious gesturing, and a general air of impatience, and if he admitted his sustained drive, competitiveness, and necessity to accelerate many activities and was aware of a chronic sense of urgency in daily living. If one or both of the latter were inconsequential, the subject was classified as exhibiting an incompletely developed behavior pattern.

Similarly, in classifying men of group B, if an individual sat relaxedly, moved slowly and calmly, exhibited no muscular tension, spoke slowly, rarely indulged in tense gestures, exhibited no impatience, and denied even moderate drive or ambition, shunned competition, avoided involvement in deadlines, and felt no sense of urgency, he was adjudged as having a completely developed behavior pattern.

The men of group C were not assessed this way because of a ubiquitous general air of resignation, worry, and hopelessness.

Survey of Dietary and Alcohol Ingestion.—The men of groups A and B were carefully instructed in the dietary diary system previously found so successful,[2] each recording daily for seven days his complete intake of food and alcohol. Individual anonymity (code numbers) was used to avoid possible reluctance to report alcohol ingestion.

The diets of men in group C were obtained in the institutionalized subjects by calculation of four weekly menus and in the remaining blind subjects by daily telephoning for seven days to determine their actual food consumption. Their average alcohol intake was obtained by direct questioning.

The dietary intakes were calculated by the chief dietitian of Mount Zion Hospital (Evelyn Piercy, B.S.), who was never informed of the identity of the dietary diaries.

Blood Studies and Cardiovascular Survey.—For determination of serum cholesterol level and blood coagulation time, each subject was bled once at 9:00-11:00 a. m. and the total serum cholesterol level analyzed in duplicate.[3] The blood coagulation time of each subject was determined according to our previously described method.[1]

TABLE 1.—*Summary of*

Pattern and Age Group, Yr Completely developed pattern	No. of Patients	Av. Age, Yr.	Av. Height, In.	Av. Weight, Lb.	Work, Hr./Wk.	Physical Activities, Hr./Wk.	Sleep, Hr./Night	Cigarettes: Smokers, %	Cigarettes: No./Day	Alcohol, Calories/ Day
30-40	14	35	69	169	53	14	7.3	71	25 (±5.9)	218
40-50	37	44	71	178	52	11	7.2	62	22 (±3.3)	229
50-60	18	54	71	182	53	8	7.5	88	32 (±3.8)	133
Av.†	69	45	71	177	52 (±3.7)	11 (±0.9)	7.3	71	26 (±2.7)	202 (±22)
Incompletely developed pattern										
30-40	4	34	74	175	47	8	7.4	50	9 (±6.2)	206
40-50	6	46	70	171	47	8	7.7	40	7 (±7.1)	176
50-60	4	54	71	165	45	6	7.5	66	20 (±9.2)	77
Av.‡	14	45	71	170	46 (±1.6)	7 (±1.3)	7.6	50	11 (±4.8)	156 (±50)
Total Av.§	83	45	71	176	51 (±1.2)	10 (±0.8)	7.3	67	23 (±2.4)	194 (±21)

* All figures in parentheses are standard errors of means.
† Av. of men of all ages exhibiting totally developed pattern.
‡ Av. of men of all ages exhibiting incompletely developed pattern.
§ Av. of all men of group A.

Detection of early or even late clinical coronary disease usually requires elicitation of a typical history of infarction or angina pectoris and/or specific electrocardiographic abnormalities. Therefore, each subject was questioned about possible rheumatic, congenital, hypertensive, or other heart disease, and then a careful history of possible infarction or angina pectoris was taken. A diagnosis of angina pectoris was entertained only if the subject had acute episodes of substernal pain with or without typical radiation, which probably could not be explained by any extracardiac ailment, if such episodes primarily occurred after exercise or emotional distress and were rapidly relieved by rest and/or nitroglycerine.

TABLE 2.—*Summary of*

Pattern and Age Group, Yr. Completely developed pattern	No. of Patients	Av. Age, Yr.	Av. Height, In.	Av. Weight, Lb.	Work, Hr./Wk.	Physical Activities, Hr./Wk.	Sleep, Hr./Night	Cigarettes: Smokers, %	Cigarettes: No./Day	Alcohol, Calories/ Day
30-40	21	34	69	172	52	5	8.0	65	16 (±4.6)	160
40-50	24	44	70	175	40	8	7.8	50	13 (±3.8)	151
50-60	14	53	69	172	41	7	8.0	21	7 (±4.2)	117
Av.†	58	43	69	173	44 (±1.2)	7 (±0.9)	8	48	13 (±2.1)	144 (±29.4)
Incompletely developed pattern										
30-40	9	35	69	162	49	6	7.8	66	18 (±6.2)	69
40-50	13	46	68	170	44	9	7.2	83	22 (±5.4)	113
50-60	3	54	73	186	41	7	8.0	66	16	456
Av.‡	25	43	69	169	45 (±1.4)	8 (±1.5)	7.5	75	20 (±2.9)	160 (±49.5)
Total Av.§	83	43	69	172	45 (±0.9)	7 (±0.2)	7.8	56	15 (±1.24)	149 (±25.4)

* All figures in parentheses are standard errors of means.
† Av. of men of all ages exhibiting totally developed pattern.
‡ Av. of men of all ages exhibiting incompletely developed pattern.
§ Av. of all men of group A.

A standard 12-lead electrocardiogram was also obtained and considered diagnostic of coronary disease only if there were characteristically abnormal T waves, not ascribable to any known extracardiac cause, or diagnostic pattern of healed infarction. The tracings were interpreted, without identification, by one of us (R. H. R.) and again by an electrocardiographer not involved in this study. Except in one instance there was complete agreement in the two series of interpretations.

We also determined the incidence of arcus senilis in the men of groups A and B by meticulous gross inspection with use of frontal and lateral flashlight illumination of the eye.

Results—General Characteristics

Group A.—As table 1 indicates, the majority of the 83 subjects in group A were adjudged as exhibiting behavior pattern A in its fully developed form. These men appeared to be "doers," capable of accomplishing their particular functions, whether these had to do with heavy construction projects, running newspapers, organizing and executing advertising campaigns, merchandising foods and beverages, or manufacturing and distributing paper products throughout the nation. Nevertheless, it was apparent that they were chronically harassed by their various commitments, ambitions, and drives. It is an oversimplification to state that their key area of harassment and major source of frustration appeared to be the seeming paucity of time itself, due to the per se disparity that existed between the things they wished or felt impelled to do and the time available for such actions.

Findings in Group A°

Dietary Data											
Total Calories	Protein	Carbohydrates	Fat	Animal Fat	Fat, % of Total Calorie Intake	Voluntary Diet Restriction, %	Positive Parental History, %	Arcus Senilis, %	Clinical Coronary Disease, %	Clotting Time, Minutes	Serum Cholesterol Level, Mg./100 Ml.
2,007	342	760	905	653	45.1	18	36	7	18	6.6 (±0.2)	240 (±8.7)
1,937	329	672	936	690	48.3	56	39	43	32	6.8 (±0.12)	263 (±8.1)
2,152	384	804	964	719	44.8	63	33	66	50	7.2 (±0.18)	259 (±7.4)
2,011 (±59)	348 (±12.4)	728 (±28.)	935 (±32)	691 (±27.)	46.5 (±0.7)	50	37	42	34	6.8 (±0.09)	257 (±4.8)
2,428	325	902	1,201	747	49.5	0	25	0	0	7.4 (±0.30)	219 (±11.1)
2,189	383	895	911	623	41.6	50	43	16	0	7.3 (±0.35)	251 (±12.2)
2,097	421	763	913	726	43.5	50	25	50	0	7.1 (±0.32)	226 (±14.2)
2,223 (±109)	381 (±47.0)	864 (±31.2)	978 (±31.6)	684 (±38.2)	44.0 (±1.5)	36	33	21	0	7.3 (±0.28)	235 (±8.3)
2,049 (±58)	354 (±13.0)	751 (±26.)	944 (±28.)	690 (±23)	46.1 (±0.6)	48	36	38	28	6.9 (±0.11)	253 (±4.3)

The second most characteristic feature of these men was their eagerness to compete not only in daily vocational business activities but also in their avocational pursuits. Closely aligned was their admitted eagerness also to win in all such activities.

Findings in Group B°

Dietary Data											
Total Calories	Protein	Carbohydrates	Fat	Animal Fat	Fat, % of Total Calorie Intake	Voluntary Diet Restriction, %	Positive Parental History, %	Arcus Senilis, %	Clinical Coronary Disease, %	Clotting Time, Minutes	Serum Cholesterol Level, Mg./100 Ml.
2,295	349	950	996	699	43.4	0	15	0	0	7.4 (0.15)	194 (±7.4)
2,138	346	797	995	678	46.5	33	21	8	0	6.9 (±0.13)	211 (±7.8)
1,975	318	678	979	597	49.6	77	38	21	0	7.3 (±0.22)	230 (±8.3)
2,163 (±53)	341 (±11.4)	830 (±25)	992 (±42.)	669 (±31.6)	45.9 (±0.9)	32	23	8	0	7.2 (±0.11)	210 (±4.7)
2,202	312	856	1,034	724	47.0	0	33	0	0	6.7 (0.14)	214 (±11.4)
2,011	322	785	904	673	45.0	28	38	23	15	6.6 (±0.12)	251 (±11.1)
1,894	267	756	871	572	45.9	100	33	33	33	6.7	223
2,058 (±59)	311 (±22)	805 (±31.4)	942 (±41)	679 (±39.2)	45.8 (±1.3)	27	36	16	11	6.6 (±0.13)	226 (±8.8)
2,134 (±55)	333 (±15.2)	823 (±27.4)	978 (±32.3)	672 (±25.4)	45.8 (±0.7)	31	27	11	4	7.0 (±0.12)	215 (±4.1)

Finally, it was noted that men 40-50 years old predominated in this group, apparently due to the fact that, in the industries selected, it is such men who are most frequently observed by their associates and superiors to exhibit the characteristic traits of behavior pattern A. This is perhaps so because, in this decade, men displaying this behavior pattern will have attained a position wherein these traits may be more readily displayed and observed. Conversely, the smaller number of men aged 50-60 years was probably due to their relative scarcity in the more active, competitive divisions of various companies and businesses.

Group B.—Despite preliminary screening of various groups of men and conscientious efforts of our lay selectors, not all of the 83 men selected for us as exhibiting overt behavior pattern B were judged by us as displaying this pattern in its fully developed form. As table 2 shows, almost half of the men between 30 and 50 years of age were not adjudged by us as exhibiting a behavior pattern completely the exact converse of pattern A. As in the men of group A, obvious signs of severe neurosis were not often observed by us, although they generally were more excited about the studies than the men of group A, due partly to the fact that annual medical examinations were the custom with men of group A and rather the exception with men of group B. Although they were more excited or apprehensive about our studies, it was obvious to the trained observer that the external behavior of those exhibiting completely developed pattern B was totally and strikingly different from that of men in group A. The most striking difference was the relative or complete absence of the sense of time urgency so prevalent in group A.

In further sharp contrast, most men of group B were obviously more content with their respective lot in life and relatively uninterested in pursuing multiple goals or competitive activities. Few appeared really concerned with advancement, and most were far more involved with their families and avocational activities.

It is of interest and perhaps of importance that the men of group B exhibiting the incompletely developed behavior pattern were so assessed not because they had greater ambition or drive but primarily because they exhibited in some degree the sense of time urgency. But, while exhibiting this trait, they differed from men of group A in not being as consciously harassed by this sense of paucity of time.

TABLE 3.—*Summary of*

Age Group, Yr.	No. of Patients	Av. Age, Yr.	Av. Height, In.	Av. Weight, Lb.	Work, Hr./Wk.	Physical Activities, Hr./Wk.	Sleep, Hr./Night	Cigarettes		Alcohol Calories/Day
								Smokers, %	No./Day	
30-40	16	34	68	147	0	10	8	77	17 (±4.4)	0
40-50	13	45	69	164	0	10	8	46	14 (±4.1)	23
50-60	17	54	69	172	0	8	9	57	7 (±2.1)	87
Av.	46	45	69	161	0	9 (±0.75)	8	61	12 (±2.7)	38 (±7.0)

* All figures in parentheses are standard errors of means.

As table 2 indicates, the greatest number of group B men were aged 40-50 years. This preponderance was purposely sought by us to provide age-paired controls for the men of group A.

Group C.—The unemployed, blind subjects in group C understandably exhibited typical signs of anxiety and insecurity. Half were learning a trade, reading, writing, and how to walk alone on city streets. These men exhibited worry and apprehension about their possible failures to earn a living. Their demeanor during our studies was neither the generally impatient one displayed by men of group A nor the somewhat apprehensive one shown by many men of group B. Previous physician contacts probably had conditioned them against fear of examinations or even venipuncture.

They were similar to group B men in not displaying any sense of time urgency, their speech, movements, and gestures being unhurried and devoid of overriding tension. None exhibited the slightest vestige of competitive drive or desire to excel. In summary, then, these subjects exhibited the behavior pattern found in men of group B, but with a universal overlay of understandable anxiety and insecurity.

Results—Subject Data

Age, Height, and Weight.—Tables 1, 2, and 3 indicate comparable age distribution in the three groups and the subdivisions of groups A and B. However, the preponderance of men 40-50 years old in groups A and B is not present in group C.

The average height of the men of group A was 2 in. (5.08 cm.) greater than that of men in group B or C, and their slightly greater average weight (4 lb. [1.8 kg.]) can be ascribed to this difference in height. The blind subjects, as a group, were less corpulent.

Work, Exercise, and Sleep Habits.—As tables 1, 2, and 3 indicate, group A men worked more hours per week (51 hours) than group B men (45 hours). (The subjects in group C were not gainfully employed.) This slight difference resulted from the men of group A beginning and ending their day's work earlier and later, respectively, than the men of group B.

Similarly (tables 1, 2, and 3), group A men were slightly more active physically (10 hours per week) than were group B men but not significantly more than the men in group C, who, surprisingly, indulged in much daily calisthenics and purposeful walking. Although certain studies have suggested that physical exercise may lower the serum cholesterol level, no such relationship was observed here (see figure). The sleep patterns of the three groups were similar.

Ingestion of Food, Tobacco, and Alcohol.—Satisfactory dietary records were obtained from 75 group A men, 76 group B men, and the 25 blind subjects who were not institutionalized. Tables 1, 2, and 3 indicate that the average dietary intakes of the men in groups A and B were approximately the same both qualitatively and quantitatively, although the average calorie intake of the blind subjects (group C) appeared to be somewhat greater. (It is believed that this is due to the fact that 21 of the 46 were fed a very liberal diet of 2,819 calories at the institution caring for them.) The percentage fat intake was comparable in all groups. Over 65% of ingested fat in each group was of animal origin. Not surprising to us[2] was the finding that the daily average calorie intake was far below that commonly assumed and that 48% of the men in group A and 31% of those in group B habitually restricted their food ingestion.

Although the percentage of group A men who smoked (67%) was not much greater than that in group B (56%) or group C (61%), the group A men smoked a daily average of 23 cigarettes, compared to 15 by group B men and 12 by group C men. Thus, group A men smoked more excessively than did men of the other two groups.

The average daily alcohol ingestion of group A men was somewhat higher than that of group B men, but the difference was not statistically significant (difference of means ÷ standard error of difference of means = 1.36). However, their average ingestion was much higher than that of the men of group C (tables 1, 2, and 3).

Parental Clinical Coronary Artery Disease.—Approximately 36% of group A men stated that either one or both parents suffered from clinical coronary artery disease. Twenty-seven per cent of group B men and 15% of group C men believed the disease present in one or both parents.

*Findings in Group C**

Dietary Data									
Total Calories	Protein	Carbohydrates	Fat	Animal Fat	Fat, % of Total Caloric Intake	Positive Parental History, %	Clinical Coronary Disease, %	Clotting Time, Minutes	Serum Cholesterol Level, Mg./100 Ml.
2,505	368	1,000	1,137	843	45.3	13	0	7.7 (±0.18)	207 (±7.8)
2,436	354	1,029	1,053	779	43.5	15	8	7.3 (±0.14)	228 (±6.6)
2,224	342	871	1,011	760	45.5	18	6	7.1 (±0.13)	226 (±8.5)
2,382 (±93)	354 (±18.6)	961 (±33)	1,067 (±61)	794 (±35.8)	44.9 (±0.8)	15	4	7.4 (±0.12)	220 (±5.2)

Serum Cholesterol Level.—The average serum cholesterol level of all the group A men was significantly higher (253 mg. per 100 ml.) than that of either group B men (215 mg. per 100 ml.) or group C men (220 mg. per 100 ml.). An even greater difference was observed by comparing the average serum cholesterol level of the men exhibiting completely developed behavior patterns in groups A, B, and C.

Blood Coagulation.—As tables 1, 2, and 3 indicate, the blind subjects in group C exhibited an average blood clotting time (7.4 minutes) that was significantly slower than that of group A men (6.9 minutes). However, the average clotting time of group B men (7.0 minutes) also was relatively rapid. Since a change in clotting time may occur very rapidly in response to various emotional stimuli,[4] it is quite possible that the acute apprehension observed in group B men at the time of the examination was itself responsible for their generally hastened clotting time. Nevertheless, when the average clotting time (6.8 minutes) of the men exhibiting fully developed pattern A was compared with that (7.2 minutes) of the men exhibiting fully developed pattern B, the difference was still significant. It was of interest, too, that the average clotting time was less than 7 minutes in 67% of the group A men, in 51% of group B men, and in only 20% of group C men.

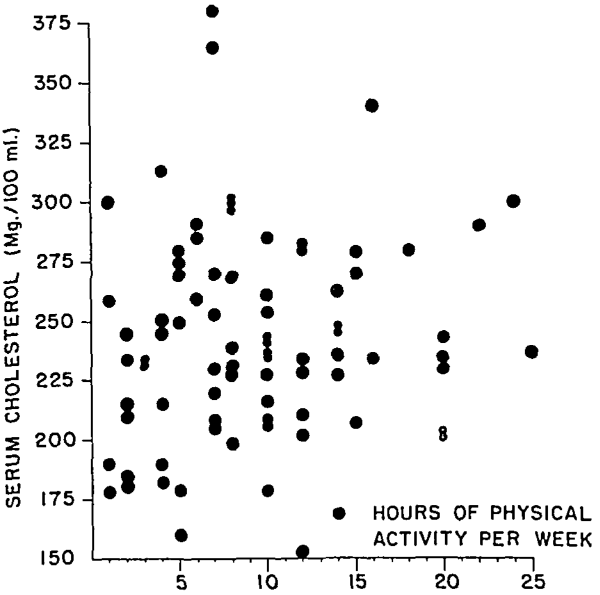
Arcus Senilis.—The difference in incidence of arcus senilis was striking (tables 1 and 2), being over three times greater in group A than in group B men. This discrepancy became five times as great when respective segments of each group exhibiting the completely developed patterns were compared. Parenthetically, it should be stated that no valid correlation was observed between the incidence of this ocular phenomenon and the level of serum cholesterol.

Results—Clinical Coronary Artery Disease

Incidence.—A marked disparity in the incidence of clinical coronary disease was found in the three groups of men selected at random and supposedly differing only in their particular overt behavior pattern. Thus (table 4), 23 group A men (28%) exhibited either clear-cut symptoms or definitive electrocardiographic signs of clinical coronary disease, findings noted in only 3 of the 83 men of group B and in only 2 of the 46 men of group C.

These results were even more striking when comparing the respective subgroups of A and B. Thus, all 23 cases of clinical coronary disease in group A were found in the men of subgroup A displaying the fully developed behavior pattern, whereas the 3 clinical instances in group B were observed in the subgroup displaying the incompletely developed pattern B.

The diagnosis of clinical coronary artery disease was made in 4 of the 23 subjects in group A by the history of typical angina, in 10 by characteristically abnormal electrocardiograms, and in 9 by a combination of history and electrocardiographic criteria. It is of interest that, of 8 of the 23 subjects with indisputable electrocardiographic evidence of healed myocardial infarction, only 4 were aware of having suffered a heart attack. These same 4 persons also were the only ones of the total of 23 who were aware of their clinical coronary disease. The remaining were completely unaware of its presence. Two of the three cases of clinical coronary disease in group B were diagnosed by electrocardiographic criteria and the third by a history of angina. One of the two cases in group C was diagnosed by history and electrocardiographic criteria and the second by electrocardiogram. Neither of the subjects in group B and only one in group C was aware of suffering from clinical heart disease.



Relationship of serum cholesterol level and exercise of men of all groups between 40 and 50 years of age.

Possible Correlation of Incidence with Other Factors.—The above findings should be a stimulus for further study, since they do not describe some biochemical deviant, having possible relevance to heart disease, but depict an overwhelming difference in heart disease incidence in groups of men selected initially only on the basis of observed differences in overt behavior patterns.

In table 4, the various data collected from subjects considered to have clinical coronary disease are assembled. Comparison of age, height, and weight of those with cardiac disease with those obtained from all subjects reveals that these factors cannot apparently be given pathogenic relevance to the question under study.

Similarly, the factors of sleep and exercise do not appear different in the 23 subjects with cardiac disease in group A. Their weekly period of working hours (52 hours) is not longer than that of all of the men of group A but is longer than that found in men of group B. That this longer period of daily work is, per se, the cause of the higher incidence of heart disease in men of group A seems unlikely, since the total national incidence of clinical coronary disease has risen over the past decades even though the number of working hours has declined. Furthermore, none of the 18 subjects in group B who had been working 50 or more hours per week exhibited clinical disease. The latter group includes a small number, but certainly if a group of 83 persons (group A) provides 23 cases of clinical disease because of long working hours, the factor(s) responsible might also be expected to produce at least one case in the 18 persons of group B also working a similar number of hours.

The dietary data indicate that the diet of men in group A, at each decade, did not differ from that of men in group B or C either in calorie intake or in the type of fat ingested. Furthermore (table 4), the men of group A with clinical heart disease who were unaware of its presence ingested quantitatively and qualitatively the same diet as that taken by other members of group A and by those of groups B and C. It seems clear that it is not the diet or any of its constituents which, acting alone and of itself, can be held responsible for the presence of so much coronary heart disease in group A men.

The greater tobacco consumption by group A men seems a possible cause of their high incidence of clinical disease, but closer inspection reveals that heavy cigarette smoking could not, per se, be responsible for the high incidence of heart disease in the men of group A. Thus, of 60 group A men smoking 10 or more cigarettes a day, 16 were found to have cardiac disease (27%), but of the 23 remaining Group A men who smoked 10 or fewer cigarettes daily, seven had cardiac disease (30%). Thus, as many light smokers or nonsmokers exhibited clinical disease as did the heavy smokers of group A. Moreover, there were 46 men of group B who smoked heavily, yet only 2 (4%) exhibited clinical coronary disease and only 1 of the 37 light smokers or nonsmokers of this group developed detectable coronary disease. The data suggest that excessive

TABLE 4.—*Summary of Findings*

Group	No. of Patients	Av. Age, Yr.	Av. Height, In.	Av. Weight, Lb.	Work, Hr./Wk.	Physical Activities, Hr./Wk.	Sleep, Hr./Night	Cigarettes Smokers, %	Cigarettes No./Day	Alcohol Calories/Day
A	23	48	71	179	52	11	7.1	69	26 (±5.2)	244 (±35.4)
B	3	46	67	174	42	7	7.0	66	13	224
C	2	47	68	185	0	10	8.0	100	30	105

* All figures in parentheses are standard errors of means.

smoking may be a characteristic of overt behavior pattern A but not a causal agent of the high incidence of cardiac disease found characteristic of this pattern.

Alcohol.—The average daily alcohol consumption of the 23 subjects with cardiac disease in group A and of the three in group B was higher than the average of their respective groups. Despite this, 12 of the 23 in group A did not drink or ingested less than the equivalent of 150 calories per day. Thus, of 44 group A men who drank little or none, 12 (27%) were found to have cardiac disease. The remaining 39 group A men who drank more included the remaining 11 with cardiac disease (28%). If the considerable ingestion of alcohol played a role in the pathogenesis of this disorder, one might expect a higher incidence of the disease in men belonging to a group given to heavy drinking. Like cigarettes, greater ingestion of alcohol in group A appears to be associated with the behavior pattern rather than of pathogenic consequence.

Parental Incidence of Coronary Artery Disease.—The apparently greater parental incidence of coronary disease in men chosen according to a prescribed psychological pattern might be blamed for their greater incidence of heart disease. However, the greater parental incidence could not be due to the behavior pattern of the men, but, rather, it is possible that these group A men had inherited some of their behavior pattern traits and it was the presence in their parents of these same traits that led to the latters' own greater incidence of cardiac disease. It was observed in a man with cardiac disease that, if his father also had suffered from coronary artery disease, the latter's personality was similar to his own. Contrariwise, in most instances where the father had not similarly suffered, the person with cardiac disease sharply differentiated his own personality from that of his father's.

*in Subjects with Cardiac Disease**

Dietary Data								Diagnosis Established by				
Total Calories	Protein	Carbohydrates	Fat	Animal Fat	Fat, % of Total Calorie Intake	Positive Parental History, %	Arcus Senilis, %	History Alone, %	ECG Alone, %	Both, %	Serum Cholesterol Level, Mg./100 Ml.	Clotting Time, Minutes
1,840 (±75)	320 (±14.2)	659 (±32)	861 (±37.2)	621 (±31)	46.8 (±1.8)	35	65	17	43	40	251 (±14.2)	6.8 (±0.14)
1,918	296	682	940	708	49.0	0	0	33	66	0	237	6.7
2,819	409	1,130	1,280	984	45.5	50	...	0	50	50	232	7.8

The data also revealed that of the 30 group A men having a positive parental history, only 8 (27%) had heart disease and of 53 men without a parental history 15 (28%) had heart disease. None of the 23 group B men with positive parental history exhibited clinical heart disease.

The data fail to incriminate differences in positive parental history between group A and B as being responsible for their markedly different incidence if clinical coronary artery disease.

Serum Cholesterol Level.—The unmistakably different average serum cholesterol level in group A and group B men might be considered responsible for the greater incidence of clinical coronary artery disease in group A. However, the average serum cholesterol level of the 19 subjects with cardiac disease in group A (the four men aware of their disorder and possibly on special diet were not included) is not significantly different from that of the total group (table 4). Second, again omitting the four with known cardiac disease, among 36 group A men with a serum cholesterol level exceeding 250 mg. per 100 ml., 10 (26%) exhibited clinical coronary disease and, of 43 having a serum cholesterol level below 250 mg. per 100 ml., 10 (23%) exhibited clinical coronary disease. Moreover, of the 14 group B men having a serum cholesterol level exceeding 250 mg. per 100 ml., only 1 exhibited clinical coronary disease. These results suggest that, as in greater working hours, smoking, and ingestion of alcohol, a comparatively higher serum cholesterol level also is an accompaniment of overt behavior pattern A rather than a cause of the higher incidence of clinical disease.

Blood Coagulation.—Although the average clotting time (6.8 minutes) of the 23 subjects with cardiac disease in group A was relatively rapid, it was similar to that of the other men in this group and only slightly more rapid than that of the subjects in group B. The data do not permit attributing the high incidence of cardiac disease in group A to an alteration in the clotting time.

However, it is likely that the incidence of thrombotic complication must have been far greater in group A than in the other groups, since the emergence of clinical coronary artery disease so often follows a thrombotic complication in an atherosclerotic coronary artery.[2] We, therefore, do not feel justified to dismiss the possible role of a chronically or episodically hastened clotting time in the pathogenesis of clinical coronary artery disease, despite the present failure to demonstrate its relevance in this regard.

Comment

The preceding observations demonstrate that men exhibiting a specific overt behavior pattern (type A) also exhibit higher serum cholesterol levels, a more rapid clotting time, a greater incidence of arcus senilis, and a far greater incidence of clinical coronary artery disease than men exhibiting converse behavioral traits or a simple anxiety state. These differences, moreover, cannot be ascribed to differences in exercise, calorie or fat intake, alcohol, or cigarettes.

The failure to detect any extraneous factor that might have induced these differences suggests that the behavior pattern itself is responsible for the changes in blood cholesterol level and cornea and coronary vasculature. Certainly, changes in blood cholesterol level and clotting time occurring in accountants exposed to one element of this behavior pattern (i. e., the involvement in deadlines), suggest that the chronic exhibition of this behavior pattern indeed can induce a sustained rise in serum cholesterol level and acceleration of blood clotting time. Groover,[5] Hammarsten and associates,[6] and Wertlake and co-workers[7] have reported similar striking elevations of the serum cholesterol level after exposure to emotional factors similar to those at play in behavior pattern A.

In view of the present data it is significant that, in studying patients with clinical coronary disease, many of them already have been found[8] to exhibit many of the qualities making up the behavior pattern under discussion. Thus, although Gertler and others,[9] in their study of 100 young patients with coronary disease, and later Miles and associates,[10] studying the same men, did not find any significant differences in their personalities, careful scrutiny of their data reveals that the majority of these 100 men actually did exhibit many of the qualities characterizing behavior pattern A. For example, their patients exhibited several times the proficiency of their controls in their high school athletic careers and were even described as "hard-driving and goal-directed."[9] A mesomorphic constitution, as these authors suggest, might explain their athletic superiority in high school but not the drive, ambition, and competitive spirit that were further needed to obtain athletic awards and the higher civil positions successfully obtained by these men in later life. It seems to us more fruitful to incriminate the cast of a personality than the contours made by muscle and bone.

The present study again points out, as Yudkin,[11] Page and associates,[12] and Yerushalmy and Hilleboe[13] previously have done, the dangers of attributing to dietary ingestion of fat alone a too preponderant role in the pathogenesis of clinical coronary artery disease. Thus, the average serum cholesterol levels of the men of groups B and C were as low, at all ages, as those of subjects[14] ingesting only half as much fat. Indeed, the lower serum cholesterol level and the markedly lower incidences of arcus senilis and clinical coronary artery disease in the men of group B, despite the equivalence of their calorie and fat intake with that of the men of group A, clearly indicate the presence of additional, perhaps far more important, factors at work in the pathogenesis of the disease.

Despite the importance of the behavior pattern itself, we believe that chronic ingestion of a high-fat diet must play an important role in the causation of clinical coronary artery disease. Our conviction is based on the simple fact that feeding excessive fat to various laboratory animals frequently induces atherosclerosis. However, the lethalness of a high fat intake for man apparently depends on an interplay with other important factors. Unfortunately, neither the mechanism by which a high fat intake experimentally increases the serum cholesterol level and induces atherosclerosis nor the mechanism by which a behavior pattern might effect the same phenomena is known. Indeed, even the mechanism responsible for control of the "normal" serum cholesterol level remains unknown. Until such mechanism can be discovered assumptions based on data other than those obtained from closely controlled studies must be viewed with extreme reserve. The investigator, moreover, must be willing to acknowledge the possible presence of pathogenic factors which cannot be measured by those instruments or techniques now available to him.

It should again be emphasized that this is a study of men exhibiting different behavior patterns and not a study of the effects of any particular type of vocational position or socioeconomic status. The recent observations of Pell and D'Alonzo[15] and Lee and Schneider[16] indicate clearly enough that the responsibility or the socioeconomic importance of the subject's position does not govern the incidence of clinical coronary disease. We suspect that a behavior pattern is the result of a specific reaction of the individual to his particular environment, in which case the pattern might be altered by a change either in the person's reaction or in his environment. In this latter respect, it is of interest that, in our previous study of accountants,[1] their behavior pattern and serum cholesterol levels (in April, during their deadline period) resembled those of men of group A but, in February (in the absence of a deadline), resembled those of men of group B.

Whatever is responsible for the behavior pattern A herein described, certainly it is neither confined to nor perhaps even more common in any particular echelon of corporate or industrial life. Actually, as Stewart[17] has emphasized, the emergence of this behavior pattern now seems to be an ubiquitous and status-transcending phenomenon in our Western society. It should be emphasized, too, that the stresses of this same society are of a variety never previously witnessed in any previous age of society, as the distinguished historians, Toynbee ("A study of History") and De Jouvenel ("Sovereignty") have pointed out. To confuse the identity and effects of these stresses with those of simple neuroses is to err, as the results of this paper demonstrate.

It appears almost mandatory in a study of this kind that the assessment of various behavior patterns actually be done by the investigators themselves, even though this decreases the number of subjects that can be studied. On the other hand, study of even thousands of subjects cannot eliminate the possible error that is introduced if such a study contains two or more variables. Thus, if only one variable is recognized and thus accorded erroneous validity, then the use of thousands may only multiply the seriousness of the error.

Summary

The possible effect of socioeconomic pressure and stress in the pathogenesis of clinical coronary artery disease was studied in men exhibiting three different overt behavior patterns. Men of group A exhibited a behavior pattern primarily characterized by intense ambition, competitive "drive," constant preoccupation with occupational "deadlines," and a sense of time urgency and the men of group B, a converse behavior pattern. Men of group C exhibited a behavior pattern essentially similar to that exhibited by men of group B, but with the added elements of a chronic anxiety state.

The total calorie and fat intake and the amount of physical activity were approximately the same in all groups, and the age, height, and weight of men in the three groups were comparable. Despite these similarities, the average serum cholesterol level was much higher in group A than in the other two groups. A hastening of blood clotting time was not observed in all men of group A, but only in those exhibiting the most fully developed form of the behavior pattern.

Far more striking, however, was the startling difference in incidence both of clinical coronary artery disease and of arcus senilis. Thus clinical coronary artery disease was seven times more frequent, and arcus senilis was over three times more frequently present in the men of group A than in those of group B or group C.

The possible role of cigarette smoking, exercise, working hours, alcohol ingestion, and heredity was studied in the pathogenesis of the cases of clinical coronary heart disease, but none, per se, appeared to have pathogenic relevance.

The results obtained in this study strongly suggest that the behavior pattern exhibited by the men of group A was of itself largely responsible not only for their higher serum cholesterol and possible hastening of clotting time but also for their markedly increased incidence of both clinical coronary artery disease and arcus senilis.

1600 Divisadero St. (15) (Dr. Rosenman).

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PROLONGED ADMINISTRATION OF CHLORPROMAZINE (THORAZINE) HYDROCHLORIDE

CLINICAL AND LABORATORY SURVEY OF FIFTY PATIENTS

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Since chlorpromazine strikingly improves the adjustment of many psychiatric patients without being truly curative, administration in many cases must be continued for years. In order to detect possible adverse effects of such prolonged medication, a study was made in 50 patients who took it for two to four years. The total amounts taken by individual patients ranged from 54 to 1,078 Gm. All patients gained weight. No evidence of renal or hepatic dysfunction was found. Amenorrhea occurred in two-fifths of the women, but sometimes menstruation was resumed without interruption or reduction of the dosage. In some patients the white blood cell count dropped as low as 3,000 per cubic millimeter of blood; but it was not necessary to interrupt the medication, because the counts returned to normal while chlorpromazine therapy continued. Three patients manifested photosensitization each year from May to October but were desensitized by repeated limited exposures to the sun. Chlorpromazine enabled these patients to remain outside of the hospital, to work, and to be reasonably comfortable in spite of the persistence of their basic illness.

Shortly after the introduction of chlorpromazine (Thorazine) hydrochloride, it was realized that this drug could cause jaundice and agranulocytosis and that some psychiatric patients would require it indefinitely. Consequently, concern was expressed about the hazards of prolonged chlorpromazine therapy, particularly its effects on the liver and the hematopoietic system. In studying this important problem, a complete laboratory survey was made on patients who had taken chlorpromazine from two to four years. The results of this laboratory evaluation and pertinent clinical observations are the basis of this report.

This group consisted of 31 women and 19 men, aged 12 to 70. In this group were 3 men under 20, 1 man and 8 women aged 20 to 29, 12 men and 13 women aged 30 to 39, 3 men and 4 women aged 40 to 49, 3 women aged 50 to 59, 2 women aged 60 to 69, and 1 woman over 70. Diagnostically, they were categorized as follows: schizophrenic–paranoid 10, catatonic 2, hebephrenic 1, simple 1, unclassified 9, chronic hypomanic 2, chronic agitated depression 1, psychoneurosis or anxiety state 9, obsessive–compulsive neurosis 8, pseudoneurotic schizophrenia 4, and hyperkinetic brain-injured child 3. Prior to taking chlorpromazine they had been ill from 1 to 20 years and had not responded to previ-

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ous psychiatric treatment, including shock therapy and psychosurgery. At the start of chlorpromazine therapy 18 were hospitalized and 32 were at home. All were considered totally incapacitated, and none had a good prognosis for recovery.

Table 1 gives the daily dosage range, the total dosage, and the duration of treatment. This reveals that the dosage requirements of patients within the same diagnostic category varied markedly. In some instances neurotics required higher doses than psychotics to obtain and maintain improvement. Thus, it is evident that chlorpromazine is used to control symptoms and not to treat a psychosis or neurosis. Because of the difference in dosage requirements, there is a corresponding variation in the total dosage taken by the patients. Minimum total dosage was 54,000 mg.; the maximum was 1,078,000 mg. Either exceeds that usually taken by patients treated with chlorpromazine. The dosage was large enough that it is reasonable to assume that any deleterious effects should be detectable.

TABLE 1.—*Dosage and Duration of Treatment with Chlorpromazine*

Case No.	Sex	Age	Diagnosis	Daily Dosage Range	Total Dosage	Duration of Treatment, Mo.
1	F	32	Pseudoneurotic schizophrenia	100-1,800 mg.	645,000	47
2	M	39	Pseudoneurotic schizophrenia	50-300 mg.	201,000	47
3	F	50	Psychoneurotic anxiety	75-300 mg.	265,000	46
4	F	29	Psychoneurotic anxiety	75-150 mg.	158,500	46
5	M	33	Schizophrenia, paranoid	100-300 mg.	207,000	46
6	M	37	Schizophrenia, paranoid	100-600 mg.	310,500	46
7	M	37	Psychoneurotic anxiety	200-600 mg.	573,000	46
8	M	15	Hyperkinetic behavior disorder	75-125 mg.	124,200	46
9	F	34	Obsessive-compulsive	75-300 mg.	236,250	45
10	M	37	Obsessive-compulsive	75-150 mg.	112,200	44
11	M	34	Obsessive-compulsive	200-2,000 mg.	1,078,000	43
12	M	49	Schizophrenia, unclassified	100-400 mg.	304,500	43
13	F	30	Obsessive-compulsive	50-150 mg.	164,000	42
14	F	58	Pseudoneurotic schizophrenia	100-300 mg.	157,500	42
15	F	70	Chronic agitated depression	100-300 mg.	151,200	42
16	F	40	Psychoneurotic anxiety	50-200 mg.	153,750	41
17	F	29	Schizophrenia, paranoid	100-250 mg.	214,000	41
18	F	29	Obsessive-compulsive	150-1,000 mg.	564,000	41
19	F	38	Schizophrenia, unclassified	200-1,200 mg.	676,500	41
20	M	38	Psychoneurotic anxiety	75-200 mg.	195,000	40
21	F	45	Schizophrenia, unclassified	100-250 mg.	155,000	40
22	M	38	Chronic hypomanic	100-400 mg.	182,000	40
23	M	28	Obsessive-compulsive	75-200 mg.	127,600	39
24	F	32	Schizophrenia, paranoid	50-200 mg.	130,000	38
25	F	26	Psychoneurotic anxiety	50-125 mg.	71,500	37
26	F	38	Schizophrenia, unclassified	100-1,200 mg.	610,500	36
27	F	28	Schizophrenia, paranoid	100-2,400 mg.	1,065,000	36
28	F	22	Psychoneurotic anxiety	100-300 mg.	173,750	35
29	F	36	Psychoneurotic anxiety	75-250 mg.	58,750	35
30	M	12	Hyperkinetic behavior disorder	50-100 mg.	143,000	34
31	M	42	Chronic hypomanic	100-300 mg.	153,000	34
32	M	32	Obsessive-compulsive	75-300 mg.	148,500	33
33	F	38	Schizophrenia, paranoid	150-300 mg.	192,000	32
34	M	47	Schizophrenia, unclassified	100-1,000 mg.	327,000	32
35	F	55	Schizophrenia, paranoid	100-150 mg.	110,000	32
36	F	42	Schizophrenia, paranoid	250-1,200 mg.	318,750	32
37	M	35	Schizophrenia, unclassified	75-200 mg.	134,400	32
38	F	34	Schizophrenia, catatonic	100-300 mg.	230,000	31
39	F	33	Schizophrenia, catatonic	50-400 mg.	116,250	31
40	F	32	Schizophrenia, unclassified	100-600 mg.	202,500	30
41	F	47	Pseudoneurotic schizophrenia	150-300 mg.	191,000	30
42	M	36	Schizophrenia, simple	100-300 mg.	130,500	29
43	M	12	Hyperkinetic behavior disorder	50-100 mg.	65,250	29
44	F	62	Obsessive-compulsive	75-125 mg.	63,000	28
45	F	29	Schizophrenia, unclassified	300-800 mg.	344,000	27
46	F	31	Schizophrenia, unclassified	150-400 mg.	165,500	26
47	F	34	Schizophrenia, paranoid	75-150 mg.	90,000	25
48	F	26	Schizophrenia, paranoid	100-1,500 mg	324,000	24
49	M	30	Schizophrenia, hebephrenic	200-1,600 mg.	432,000	24
50	F	69	Psychoneurotic anxiety	50-100 mg.	54,000	24

Laboratory Investigation

Prior to, at repeated intervals during, and at the beginning of this survey, each patient had a urinalysis, hematological studies (red blood cell count, hemoglobin level determination, white blood cell count, and differential count), and liver function tests (cephalin flocculation, direct and indirect bilirubin, alkaline phosphatase, and, occasionally, thymol turbidity). Pretreatment and survey urinalysis were all within the range of normal variations. Urine bilirubin determination was negative in all cases.

TABLE 2.—*Hematological Data on Patients on Chlorpromazine Therapy*

Case, No.	Sex	Age	Date	Red Blood Cell Count, Million/Cu. Mm.	Hemoglobin Level, %	White Blood Cell Count, per Cu. Mm.	Polymorphonuclear Cells, %	Lymphocytes, %	Monocytes, %	Eosinophils, %	Basophils, %
1	F	32	2/ 1/54	5.1	100	6,400	61	36	2	1	..
			1/20/58	5.2	100	7,150	63	34	2	1	..
2	M	39	6/23/54	4.2	92	9,100	50	48	2	..	..
			6/30/58	4.4	96	10,500	48	41	2	3	..
3	F	50	2/ 8/54	5.1	96	6,300	60	37	2	1	..
			12/ 2/57	4.4	90	5,000	56	36	6	2	..
4	F	29	2/17/54	5.0	100	8,350	60	35	3	2	..
			12/30/57	5.1	100	9,200	63	34	2	1	..
5	M	33	2/ 4/54	5.1	100	7,600	64	35	1	..	..
			12/10/57	4.8	96	9,100	59	37	3	1	..
6	M	37	1/26/54	5.0	98	5,250	58	38	4	..	..
			11/29/57	5.2	100	7,400	66	28	4	2	..
7	M	37	2/ 5/54	5.0	98	7,800	65	27	6	2	..
			12/30/57	5.1	100	7,100	64	30	3	3	..
8	M	15	1/31/54	5.1	100	6,300	60	38	1	..	1
			11/29/57	5.01	100	7,100	42	53	3	..	2
9	F	34	5/ 1/54	4.5	90	4,400	48	45	7	..	..
			1/20/58	4.65	92	7,600	66	28	4	2	..
10	M	37	4/ 2/54	5.1	98	8,200	59	34	4	2	1
			1/ 2/58	5.2	100	7,450	64	31	3	2	..
11	M	34	2/ 1/54	5.2	100	6,400	61	32	4	2	1
			9/28/57	5.5	102	7,200	69	24	5	2	..
12	M	49	6/18/54	5.0	100	9,800	64	31	3	1	1
			1/30/58	5.1	98	6,800	60	32	7	1	..
13	F	30	4/ 6/54	5.0	92	5,400	60	36	3	1	..
			10/22/57	4.65	90	6,350	61	32	6	1	..
14	F	58	4/ 1/54	4.8	94	6,100	60	35	4	1	..
			12/31/57	4.75	92	5,400	64	32	3	1	..
15	F	70	4/ 4/54	4.8	94	6,350	64	30	3	3	..
			12/30/57	5.2	100	8,200	69	25	5	1	..
16	F	40	5/ 7/54	4.6	90	7,500	60	37	2	1	..
			10/31/57	4.25	84	6,000	61	33	4	2	..
17	F	29	1/21/55	4.3	100	6,300	62	36	2	..	..
			6/17/58	4.4	100	7,800	66	31	2	1	..
18	F	29	12/20/54	4.2	100	5,600	60	38	2	..	..
			5/18/58	4.1	100	7,100	71	28	1	..	..
19	F	38	7/21/54	4.28	84	10,100	66	33	..	1	..
			12/30/57	4.1	92	9,400	64	33	2	1	..
20	M	38	4/ 1/54	4.8	98	9,800	59	38	4	1	..
			8/ 2/57	4.9	96	11,750	56	43	0	1	..
21	F	45	6/ 5/54	4.6	100	6,900	60	38	2	..	..
			10/10/57	4.4	88	7,750	62	31	6	1	..
22	M	38	9/ 1/54	5.5	102	6,800	64	32	2	2	..
			1/24/57	5.1	105	5,600	62	34	4	..	..
23	M	28	7/16/54	5.2	100	7,200	63	34	2	1	..
			10/24/57	5.1	100	5,100	60	32	8	..	..
24	F	32	5/ 5/55	4.3	92	7,600	62	34	4	..	..
			7/11/58	4.65	90	9,100	68	30	2	2	..
25	F	26	5/23/55	4.35	94	6,200	58	40	2	..	..
			6/14/58	4.8	96	4,850	56	40	3	1	..
26	F	38	9/24/54	3.5	82	11,400	58	38	2	2	..
			10/ 1/57	3.8	88	12,700	77	19	4	..	..
27	F	28	5/ 7/55	4.3	90	8,100	60	36	3	1	..
			4/25/58	5.1	100	9,200	71	24	4	1	..
28	F	22	1/24/55	4.32	88	9,950	62	34	2	2	..
			1/ 3/58	4.0	91	11,600	65	24	3	3	2
29	F	36	2/ 8/55	4.4	94	5,700	62	34	2	1	1
			1/20/58	5.0	100	9,150	60	35	4	1	..
30	M	12	11/23/54	4.8	100	6,400	60	36	3	1	..
			9/27/57	5.0	98	5,100	44	48	7	1	..
31	M	42	3/21/55	5.0	100	5,900	58	38	2	2	..
			1/16/58	5.1	98	8,100	65	32	2	1	..
32	M	32	12/11/54	5.3	100	5,900	64	32	2	1	1
			9/27/57	5.5	102	6,600	62	32	6	..	..
33	F	38	2/26/55	5.0	100	10,200	64	32	2	1	1
			10/28/57	5.4	102	16,900	77	19	4	..	..
34	M	47	1/28/55	5.0	100	5,600	58	40	2	..	..
			9/26/57	5.2	100	6,950	61	33	4	2	..
35	F	55	4/ 9/55	5.2	98	7,000	63	36	2	1	..
			12/18/57	5.0	100	7,650	60	35	2	2	1
36	F	42	10/21/55	4.5	100	10,700	69	24	4	3	..
			6/18/58	5.1	100	8,300	64	30	4	2	..
37	M	35	5/19/55	4.3	96	7,600	60	36	3	1	..
			1/18/58	4.7	93	6,200	64	35	1	..	..
38	F	34	3/28/55	4.8	98	9,650	64	33	2	1	..
			10/28/57	5.0	100	12,800	71	20	5	4	..
39	F	33	5/25/55	4.6	94	5,800	58	36	3	1	2
			12/30/57	4.91	98	7,400	61	37	2	..	..

TABLE 2.—*Hematological Data on Patients on Chlorpromazine Therapy*—Continued

Case, No.	Sex	Age	Date	Red Blood Cell Count, Million/Cu. Mm.	Hemoglobin Level, %	White Blood Cell Count, per Cu. Mm.	Polymorphonuclear Cells, %	Lymphocytes, %	Monocytes, %	Eosinophils, %	Basophils, %
40	F	32	5/26/55 11/21/57	4.62 4.8	100 96	7,150 5,000	61 57	37 36	1 5	1 2	.. ..
41	F	47	11/15/55 5/30/58	4.0 4.2	80 96	9,500 13,200	76 77	24 21	.. 1	.. ..	.. ..
42	M	36	6/ 8/55 11/ 7/57	5.0 5.1	100 98	7,400 5,600	60 48	36 41	3 11	1 ..	.. ..
43	M	12	4/11/55 9/30/57	5.1 5.0	100 100	7,200 5,950	60 63	37 33	2 3	1 1	.. ..
44	F	62	7/ 9/55 11/12/57	3.9 4.6	80 96	5,200 8,600	58 64	37 34	3 2	2 ..	.. ..
45	F	29	7/16/55 10/29/57	4.3 4.69	82 96	6,100 4,250	55 62	40 36	1 1	4 ..	.. 1
46	F	31	8/16/55 10/10/57	5.0 3.7	98 80	7,400 9,650	62 83	37 16	1 1	.. ..	.. ..
47	F	34	11/20/55 12/ 2/57	4.6 4.9	98 97	10,200 8,350	71 62	28 36	1 2	.. ..	.. ..
48	F	26	1/ 2/56 1/ 7/58	4.12 4.0	96 96	8,400 9,150	64 58	34 38	.. 4	2 ..	.. ..
49	M	30	10/ 1/55 10/ 8/57	5.0 5.0	100 98	9,000 7,000	61 69	37 25	1 3	1 3	.. ..
50	F	69	10/ 4/55 10/29/57	5.0 4.60	96 92	5,200 3,000	58 36	40 51	2 12	.. 1	.. ..

Results of hematological studies are given in table 2. Repeated white blood cell counts and differential counts during therapy disclosed fluctuations in the total white blood cell count and the total number of neutrophils. In some patients, the white blood cell count dropped as low as 3,000, with 30 neutrophils and with a return to normal as therapy with chlorpromazine was continued. It is not necessary to discontinue the therapy when the white blood cell count and neutrophil count begin to fall. In such instances the physician should rely on his clinical judgment, in addition to the laboratory studies, to determine his course of action.

Table 3 presents the liver function studies. Only the cephalin flocculation test showed changes in some patients. A summary of these changes is given in table 4. The results are not significant (table 5). Whether they are due to chlorpromazine or other causes is unknown. In two patients there was a history of virus infection with liver involvement prior to chlorpromazine therapy and of a chronic alcohol problem with periodic heavy drinking while taking chlorpromazine. In these two cases it was felt that factors other than chlorpromazine therapy could be responsible for the changes in the cephalin flocculation tests.

All major laboratory test results were analyzed for any significant change which might have occurred. The mechanism employed was the Student's *t* test (table 5). The values of *t* are far below those which would indicate a significant difference between the pretreatment test results and survey test results.

Clinical Observations

Body Weight.—One of the most constant endocrine actions of chlorpromazine is that which affects the weight of patients receiving it. Every patient gained from 20 to 54 lb. (9.1 to 24.5 kg.), the average being 35 lb. (15.9 kg.), irrespective of the pretreatment weight. Four patients gained 20 to 25 lb. (9.1 to 11.3 kg.); 8, 25 to 30 lb. (11.3 to 13.6 kg.); 15, 30 to 35 lb. (13.6 to 15.9 kg.); 13, 35 to 40 lb. (15.9 to 18.1 kg.); 8, 40 to 45 (18.1 to 20.4 kg.); 1, 45 to 50 lb. (20.4 to 22.7 kg.); and 1, 50 to 54 lb. (22.7 to 24.5 kg.).

In the first four months of treatment patients gained weight rapidly, usually two-thirds of their total weight increase. In the next 6 to 10 months, they gradually added the remaining one-third of their total weight gain. Thereafter, their weight remained relatively constant. If dosage was lowered or the drug therapy stopped, a gradual weight loss followed but weight remained well above the pretreatment level. The photographs in the illustration show the considerable weight change in one patient.

Menstrual Changes.—The menstrual changes observed were disruption of rhythm, menorrhagia, hypermenorrhea, hypomenorrhea, and amenorrhea. The menstrual variations usually began after two weeks of therapy. In some patients the drug produced early onset of menses; in others it was delayed. Amenorrhea occurred in two-fifths of the women receiving 500 mg. or more daily. The higher the dosage used the more likely was amenorrhea to occur. As the dosage was lowered, the menses

TABLE 3.—*Results of Liver Function Tests in Patients on Chlorpromazine Therapy*

Case No.	Sex	Age	Date	Cephalin Flocculation	Serum Bilirubin, Direct	Serum Bilirubin, Indirect, Mg./100 Cc.	Alkaline Phosphatase Level, Units/-100 Cc.	Thymol Turbidity, Units
1	F	32	2/ 1/54	0-0	0	0.5	2.0	..
			1/20/58	0-0	0	0.4	1.8	..
2	M	39	6/23/54	1+-1+	0	1.0	2.6	2
			6/30/58	2+-3+	0	1.0	2.4	3
3	F	50	2/ 8/54	0-0	0	0.3	2.2	..
			12/ 2/57	0-0	0	0.2	1.8	..
4	F	29	2/17/54	0-0	0	0.4	1.6	2
			12/30/57	0-1+	0	0.8	1.8	2
5	M	33	2/ 4/54	0-0	0	0.8	1.5	..
			12/10/57	0-0	0	0.4	2.4	..
6	M	37	1/26/54	0-0	0	0.6	1.8	..
			11/29/57	1+-1+	0	0.84	1.0	..
7	M	37	2/ 5/54	0-1+	0	0.3	2.0	..
			12/30/57	0-2+	0	0.25	1.0	..
8	M	15	1/31/54	0-0	0	0.4	2.0	..
			11/29/57	0-0	0	0.22	2.2	..
9	F	34	5/ 1/54	0-0	0	0.5	1.7	..
			1/20/58	0-0	0	0.3	1.5	..
10	M	37	4/ 2/54	0-0	0	0.4	2.9	..
			1/ 2/58	0-0	0	0.5	3.4	..
11	M	34	2/ 1/54	0-0	0	0.6	3.2	3
			9/28/57	0-0	0	0.7	3.5	4
12	M	49	6/18/54	0-0	0	0.4	1.7	..
			1/30/58	0-0	0	0.3	1.9	..
13	F	30	4/ 6/54	0-1+	0	0.4	2.0	..
			10/22/57	2+-2+	0	0.4	1.6	..
14	F	58	4/ 1/54	0-0	0	0.4	1.6	..
			12/31/57	0-0	0	0.3	5.2	..
15	F	70	4/ 4/54	0-0	0	0.4	1.8	..
			12/30/57	0-0	0	0.5	1.6	..
16	F	40	5/ 7/54	0-1+	0	0.4	3.2	..
			10/31/57	2+-2+	0	0.4	2.6	..
17	F	29	1/21/55	0-0	0	0.4	1.0	..
			6/17/58	0-0	0.05	0.3	1.2	..
18	F	29	12/20/54	0-0	0	0.4	1.8	..
			5/18/58	0-0	0	0.6	2.6	..
19	F	38	7/21/54	0-0	0	0.6	2.8	..
			12/30/57	0-0	0	0.8	3.2	..
20	M	38	4/ 1/54	0-0	0	0.3	1.7	2
			8/ 2/57	0-1+	0	0.7	2.0	3
21	F	45	6/ 5/54	0-0	0	0.4	1.8	..
			10/12/57	0-0	0	0.6	1.4	..
22	M	38	9/ 1/54	0-0	0	0.4	2.0	2
			1/24/57	0-0	0	0.5	1.7	4.1
23	M	28	7/16/54	0-0	0	0.5	2.0	..
			10/24/57	0-0	0	0.4	2.5	..
24	F	32	5/ 5/55	0-0	0	0.3	1.5	..
			7/11/58	0-0	0	0.4	1.6	..
25	F	26	5/23/55	0-0	0	0.8	2.0	..
			6/14/58	0-1+	0	0.8	1.5	..
26	F	38	9/24/54	0-0	0	0.4	3.2	..
			10/ 1/57	0-0	0	0.6	2.6	..
27	F	28	5/ 7/55	0-0	0	0.6	1.9	1
			4/25/58	0-0	0	0.5	1.7	2
28	F	22	1/24/55	0-0	0	0.4	1.5	3
			1/ 3/58	0-0	0	0.4	1.8	2
29	F	36	2/ 8/55	0-0	0	0.4	1.9	..
			1/20/58	0-0	0	0.6	2.4	..
30	M	12	11/23/54	0-0	0	0.6	2.0	..
			9/27/57	0-1+	0	0.8	2.9	..
31	M	42	3/21/55	0-0	0	0.6	2.0	..
			1/16/58	0-0	0	0.4	2.6	..
32	M	32	12/11/54	0-0	0	0.6	2.5	..
			9/27/57	0-0	0	0.9	2.0	..
33	F	38	2/26/55	0-1+	0	0.4	..	..
			10/28/57	1+-1+	0	0.4	..	..
34	M	47	1/28/55	0-0	0	0.4	1.5	..
			9/26/57	0-0	0	0.5	1.8	..
35	F	55	4/ 9/55	0-0	0	0.5	1.8	..
			12/15/57	0-0	0	0.4	2.0	..
36	F	42	10/21/55	0-0	0	0.5	1.8	..
			6/18/58	0-0	0	0.4	2.0	..
37	M	35	5/19/55	0-0	0	0.3	1.4	..
			1/18/58	0-0	0	0.5	1.8	..
38	F	34	3/28/55	0-0	0	0.4	1.8	..
			10/28/57	0-1+	0	0.2	2.0	..
39	F	33	5/25/55	0-0	0	0.6	1.8	..
			12/30/57	0-0	0	0.4	1.4	..
40	F	32	5/26/55	0-0	0	0.6	1.8	..
			11/21/57	0-0	0	0.8	1.52	..
41	F	47	11/15/55	0-0	0	0.4	2.4	3
			5/30/58	0-0	0	0.5	1.4	3
42	M	36	6/ 8/55	0-0	0	0.4	2.0	..
			11/ 7/57	0-0	0	0.8	1.6	..
43	M	12	4/11/55	0-0	0	0.5	3.8	..
			9/30/57	0-0	0	0.4	4.4	..
44	F	62	7/ 9/55	0-0	0	0.8	2.0	3
			11/12/57	0-0	0	0.6	2.4	3
45	F	29	7/16/55	0-0	0	0.4	2.6	..
			10/27/57	0-1+	0	0.75	2.9	..
46	F	31	8/16/55	0-0	0	0.5	3.5	..
			10/19/57	0-0	0	0.9	3.0	..
47	F	34	11/20/55	0-1+	0	0.6	1.8	..
			12/ 2/57	1+-1+	0	0.55	1.5	..
48	F	26	1/ 2/56	0-0	0	0.4	3.0	..
			1/ 7/58	0-0	0	0.6	2.6	..
49	M	30	10/ 1/55	0-0	0	0.4	1.6	..
			10/ 8/57	0-0	0	0.4	1.4	..
50	F	69	10/ 4/55	0-0	0	0.4	1.6	..
			10/29/57	0-0	0	0.3	1.9	..

returned. When amenorrhea happened, it varied from three months to two years, the average being six months.

Photosensitivity.—Three patients were photosensitive. There was no relation between this sensitivity and the dosage of chlorpromazine. This reaction was seasonal, occurring from May to October, when the patients were exposed to the summer sun. Repeated limited exposure to the sun desensitized the patients, but the reaction recurred each year.

TABLE 4.—*Cephalin Flocculation Test*

Pretreatment	Survey	Patients, No.
0 — 0	0 — +1	6
0 — 0	+1 — +1	1
0 — +1	+1 — +1	2
0 — +1	0 — +2	1
0 — +1	+2 — +2	2
+1 — +1	+2 — +3	1
Total		13

Comment

None of the patients in this study have recovered from their basic illness, although all have shown symptomatic improvement. The 18 hospitalized patients are now at home; 4 are gainfully employed, and 7 have resumed responsibility for their household duties. Of the 32 nonhospitalized patients, 11 have returned to work and 14 are helping with the household work. It is certain that without chlorpromazine therapy most of these patients would have gradually deteriorated and would now be hospitalized. Instead, chlorpromazine therapy has enabled them to remain outside of a hospital, to work, and to be reasonably comfortable in spite of the persistence of their basic illness.

TABLE 5.—*Comparison of Pretreatment and Survey Laboratory Results in Fifty Patients*

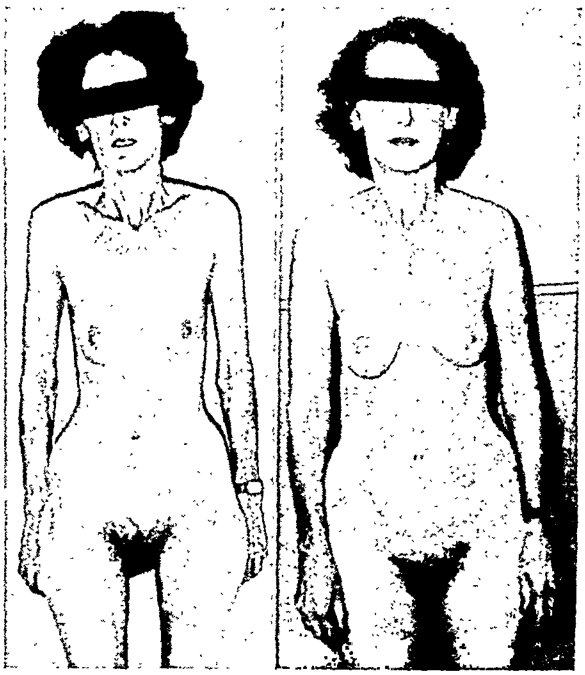
	Mean		
Test Results	Pretreatment	Survey	Value of t*
Red blood cell count, million/cu. mm.	4.7	4.8	0.017
White blood cell count, per cu. mm.	7,600	8,300	0.27
Polymorphonuclear cells, total	4,720	5,470	0.30
Cephalin flocculation			
24-hr. reading	0.03	0.29	0.49
48-hr. reading	0.17	0.52	0.45
Bilirubin, indirect	0.51	0.57	0.94
Alkaline phosphatase level, units per 100 cc.†	2.16	2.32	0.15
Thymol turbidity units‡	2.4	2.8	0.40

* Determined in Student's *t* test.
† Alkaline phosphatase level was determined in only 49 patients.
‡ Thymol turbidity determination was made in only nine patients.

These patients have continued on maintenance therapy with chlorpromazine because each time an effort was made to withdraw the drug there was a resurgence of former symptoms. Even the maintenance dose has had to be flexible. For some patients it has been necessary occasionally to increase their dosage temporarily when they encountered more environmental stress than usual.

Summary and Conclusions

Chlorpromazine (Thorazine) hydrochloride has been administered from two to four years to 50 psychiatric patients who had not benefited from previous treatment and who had a poor prognosis. These patients took from 54,000 to 1,078,000 mg. A comparison of their pretreatment and survey urinalysis and hematological and liver function studies did not reveal any significant changes. Every patient gained from 20 to 54 lb. (9.1 to 24.5 kg.), usually during the first year of chlorpromazine therapy, after which the weight remained constant. Amenorrhea occurred in two-fifths of the women. Its duration varied with the dosage of chlorpromazine. Lowering the dosage restored normal menses if normality did not return of itself. Photosensitive reactions occurred in the same three patients each year.



Weight change in patient on chlorpromazine therapy. *Left,* pretreatment weight, 80 lb. (36.3 kg.). *Right,* weight 90 days later, 109.5 lb. (49.6 kg.), after therapy with 125 mg. of chlorpromazine daily. Weight at end of one year was 115 lb. (52.1 kg.) and during next three years varied from 110 to 118 lb. (49.9 to 53.5 kg.).

It is concluded that chlorpromazine can be administered for prolonged periods, even in large doses, without the risk of harmful effects on the blood, liver, or kidneys. Prolonged therapy does not cure. It enables patients to remain outside of the hospital, to work, and to be reasonably comfortable in spite of the persistence of their basic illness.

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DIFFUSE PULMONARY SCHISTOSOMIASIS

REPORT OF TWO CASES PROVED BY LUNG BIOPSY

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and
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Two patients with signs and symptoms of chronic pulmonary disease were hospitalized because of the suspicion of tuberculosis. In one a lung biopsy specimen obtained at exploratory thoracotomy was found to contain lesions characteristic of pulmonary schistosomiasis, and ova of Schistosoma mansoni were identified. In the other the ova of S. mansoni were first found in the feces; later the characteristic ova were also found in pseudotubercules in specimens of lung tissue obtained by wedge biopsy. The first patient was treated with a total of 90 cc. of stibophen (Fuadin) injected intramuscularly over a period of 20 days, and the disease was arrested. The other improved after two courses consisting altogether of 95 cc. of stibophen; although he continued to complain of respiratory symptoms he returned to duty. Both had lived in Puerto Rico before entering the U. S. Army.

Pulmonary schistosomiasis was first described by Belleli,[1] in 1885, and since then other authors have described in detail the clinical and pathological features. Since schistosomiasis is not endemic to the United States, physicians in this country are not likely to include it in the differential diagnosis of lung diseases. In recent years large numbers of people have migrated to the United States from Puerto Rico, where the disease is endemic. A number of these persons can be expected to have pulmonary schistosomiasis, which is easily confused with tuberculosis, histoplasmosis, sarcoidosis, pneumonoconiosis, or eosinophilic granuloma.

Report of Cases

Case 1.—A 22-year-old male Puerto Rican soldier was admitted to the tuberculosis section of Fitzsimons Army Hospital on Feb. 23, 1954, because of diffuse pulmonary infiltrates.

He had lived in Puerto Rico until he entered the U. S. Army in March, 1953. In April, 1953, he was transferred to the United States where he has since remained, residing in Kansas, Texas, Louisiana, Colorado, and Illinois. Before entering the Army he was employed as a steelworker for two years. There is no record of how or when he became infected with schistosomes. His medical history was unremarkable except for an appendectomy at the age of 19. Three months prior to hospitalization he developed a cough productive of brownish-black sputum. This was most prominent at night and was only slightly improved by cough medication. No diagnostic studies were done until January, 1954, at which time he complained of some weakness but denied having hemoptysis, night sweats, or chest pain. A chest roentgenogram showed diffuse infiltrates and he was hospitalized because of the suspicion of tuberculosis.

On the physical examination given at admission he appeared well nourished and in no distress. Blood pressure was 142/90 mm. Hg, respirations 24 per minute. There was no clubbing of fingers or toes. Scattered inspiratory rales were audible over both lungs. The examination results were otherwise normal. Results of laboratory studies were as follows: serologic test for syphilis, negative; urinalysis, normal; hemoglobin level, 16.5 Gm. per 100 cc.; white blood cell count, 11,000 per cubic millimeter with neutrophils, 58%; lymphocytes, 32%; and eosinophils, 10%. Subsequently, the eosinophil counts ranged between 5 and 9%. The total serum protein level was 8.2 Gm. per 100 cc., with albumin, 3.7 Gm. and globulin, 4.5 Gm. Liver function studies done on separate occasions showed sulfobromophthalein (Bromsulphalein) retentions of 6.2, 3.0, and 8.0%. The thymol turbidity and cephalin flocculation were normal on each determination. The second-strength purified protein derivative (PPD) skin test gave a positive result. Results of coccidioidin and histoplasmin skin tests were negative in all dilutions including 1:10. Serologic tests for histoplasmosis, blastomycosis, and coccidioidomycosis obtained on March 3 and April 9 all gave negative results, except that on the first determination the result of the collodion agglutination test for histoplasmosis was positive in a dilution of 1:40. Cultures of gastric and bronchial washings were negative for Mycobacterium tuberculosis and fungi. A bone marrow culture was negative for Histoplasma capsulatum. Stool specimens initially contained ova of Schistosoma mansoni and hookworm and the rhabditiform larvae of Strongyloides stercoralis.

Pulmonary function studies on April 29th yielded the following results: Vital capacity, 2,600 cc. or 61% of the predicted normal; one-second vital capacity 2,200 cc. or 85% of the observed; maximum breathing capacity, 75 liters per minute or 53% of the predicted normal.

Roentgenograms of the chest (fig. 1) showed diffuse miliary infiltrations involving all lobes of both lungs, with scattered coalescent nodules measuring up to 5 mm. in diameter. In addition, there was a reticular pattern of increased lung markings. Serial roentgenograms throughout the period of hospitalization remained stable. A miniature film made in March, 1953, showed normal findings.

Bronchoscopy revealed a mild, diffuse hyperemia and edema of the tracheobronchial tree. A needle biopsy of the liver was performed and on microscopic examination the liver architecture was essentially normal with only a small focal area of fibrosis. A lung biopsy specimen, obtained at exploratory thoracotomy on May 18, contained lesions characteristic of pulmonary schistosomiasis. Frequent large

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From the departments of medicine and pathology, Fitzsimons Army Hospital, Denver.

ocal granulomatous areas were present, composed of fibroblasts, histiocytes, eosinophils, and occasional lymphocytes and plasma cells. In these areas were seen arteries with destruction of the muscular coat and varying degrees of obliterative endarteritis. No angiomatoid formation was found. Ova were not observed within these granulomas, but they were seen within organized pseudotubercles located in nearby alveolar spaces (fig. 2). The remainder of the pulmonary parenchyma appeared normal.

This patient presented a perplexing diagnostic problem; after tuberculosis was excluded as a diagnostic possibility, histoplasmosis and sarcoidosis were seriously considered. When ova of S. mansoni were found in the lung biopsy specimen as well as the stools all of the confusing features could be easily explained. At operation the surgeon palpated firm nodules measuring 2 to 6 mm. throughout the entire lung. There were no postoperative complications.

The patient was treated with a total of 90 cc. of stibophen (Fuadin) injected intramuscularly between June 21 and July 10. This produced some nausea, anorexia, and vomiting but did not necessitate discontinuance of the therapy. Hexylresorcinol was given for the hookworm and gentian violet for the strongyloides infections. At the completion of treatment his stools no longer contained ova and parasites. He returned to duty in August, 1954, and was subsequently discharged from the Army.

A follow-up evaluation was accomplished at the Veterans Administration West Side Hospital, Chicago, during December, 1955, and January, 1956. At that time the patient complained of shortness of breath on exertion but denied any other pulmonary symptoms. No significant physical abnormalities were found. The routine laboratory studies gave normal results, except for 9% eosinophils in a peripheral blood smear. A total circulating eosinophil count was 482 per cubic millimeter. Stool examinations revealed ova of hookworm but none of S. mansoni. A sulfobromophthalein test showed 3.5% retention. The total serum protein level was 7.8 Gm. per 100 cc., with albumin, 4.7 Gm., and globulin, 3.1 Gm. The vital capacity was 2,800 cc. and the one-second vital capacity 2,400 cc. Only a few minute petechiae of the rectal mucosa were seen on proctoscopic examination. Results of chest roentgenograms had not changed significantly. At the time of his latest follow-up, in April, 1958, he was employed and asymptomatic.

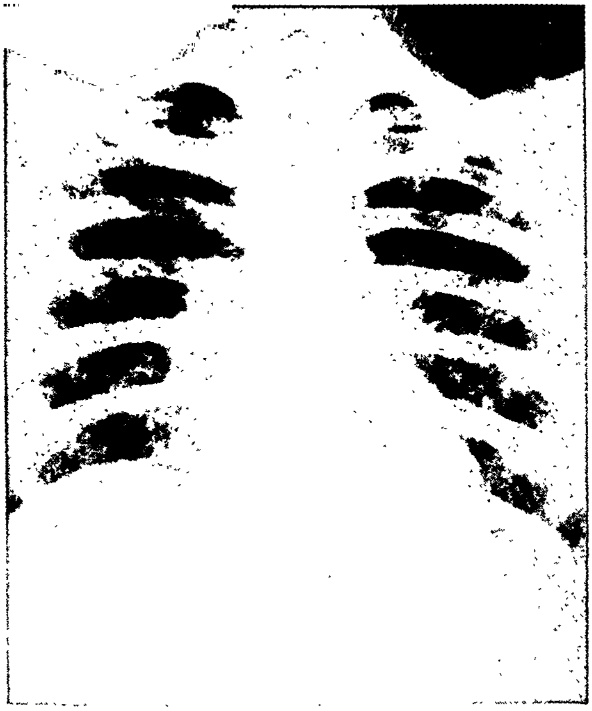

Fig. 1 (case 1).—Chest roentgenogram showing diffuse infiltrates of lungs.

Case 2.—This 20-year-old Puerto Rican male soldier was admitted to the tuberculosis section on April 30, 1957, because of a diffuse lung disease. Experience with the previous case led to a clinical diagnosis of pulmonary schistosomiasis which was confirmed by lung biopsy.

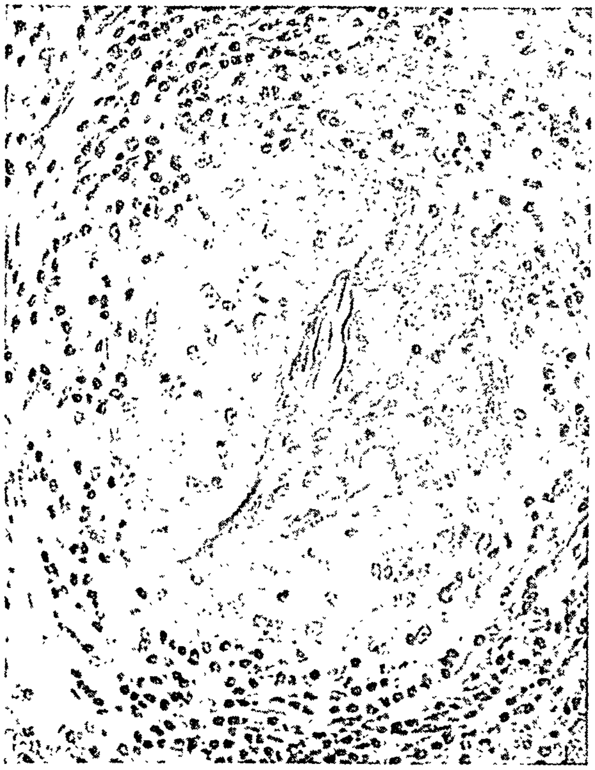

Fig. 2 (case 1).—Photomicrograph of lung biopsy specimen. Clear area within giant cell represents fragment of ovum.

The patient was born and lived in the vicinity of Comerio, Puerto Rico, until entering the U. S. Army in September, 1955. It could not be determined specifically when he contracted schistosomiasis. He was transferred to the United States in November, 1955, and was subsequently stationed at Fort Chaffee, Arkansas, and Fort Sill, Oklahoma.

He spent a 30-day leave at his home in Puerto Rico during December, 1956, and January, 1957. Three weeks after his return he developed a headache, mild fever, malaise, nonproductive cough, sore throat, and diffuse anterior chest pain aggravated by coughing. He was hospitalized at Fort Sill on Feb. 18, 1957, where at physical examination he appeared mildly ill. Temperature was 99.4 F; pulse, 80 per minute; blood pressure, 118/84 mm. Hg; respirations, 16 per minute. The pharynx was moderately inflamed and there was lymphoid hyperplasia. Auscultation over the lungs revealed diffuse inspiratory and expiratory wheezes. Scattered moist rales were localized in both lower lungs. The examination was otherwise normal. The white blood cell count was 9,000 per cubic millimeter with 59% neutrophils, 35% lymphocytes, 2% monocytes, and 4% eosinophils. Hemoglobin level was 15.3 Gm. per 100 cc., and erythrocyte sedimentation rate 16 mm. per hour. Chest roentgenograms showed diffuse infiltrative densities in both lungs. He was treated with antibiotics for one week after which the symptoms and physical findings cleared but the roentgenographic abnormalities persisted.

On his arrival at Fitzsimons Army Hospital he was asymptomatic and the results of the physical examination were essentially normal. The lungs were clear on auscultation and neither the liver nor the spleen was palpable. A repeat white blood cell count showed 11,000 per cubic millimeter, with 54% neutrophils, 38% lymphocytes, 3% monocytes, and 5% eosinophils. Hemoglobin level was 14.8 Gm. per 100 cc., and erythrocyte sedimentation rate 23 mm. per hour. Result of a serologic test for syphilis was negative. Urinalysis was normal. Results of liver function studies were normal except for a thymol turbidity of 7 units. Total serum protein level was 8.4 Gm. per 100 cc., with albumin, 3.2 Gm. and globulin 5.2 Gm. The electrophoretic pattern of the serum proteins was albumin, 42.5%; alpha-1 globulin, 4.9%; alpha-2 globulin, 14.7%; beta globulin, 16.9%; and gamma globulin, 21.0%. Results of the histoplasmin test and the second-strength PPD skin test were positive; result of the coccidioidin test was negative. Results of the histoplasmin complement-fixation test were positive in titers of 1:8 and 1:16 on separate tests. Results of the serologic tests for blastomycosis and coccidioidomycosis were negative. Repeated gastric washings disclosed no M. tuberculosis or fungi. Ova of S. mansoni were found in the stools but none could be recovered in the sputum even after the administration of expectorants. A scalene node biopsy gave normal results. Serial sections of a needle biopsy of the liver showed occasional poorly circumscribed pseudotubercles in the portal areas. Several of these pseudotubercles contained fragments of egg shell within foreign body giant cells. A wedge biopsy of the right lung, obtained July 22, showed frequent small and medium-sized histiocytic granulomatous areas containing numerous eosinophils. The small bronchi and blood vessels wit these areas were necrotic. Early fibrosis was present. Fr quent pseudotubercles containing ova were seen; one ov had a prominent lateral spine, positively identifying it S. mansoni (fig. 3). No angiomatoids were found.

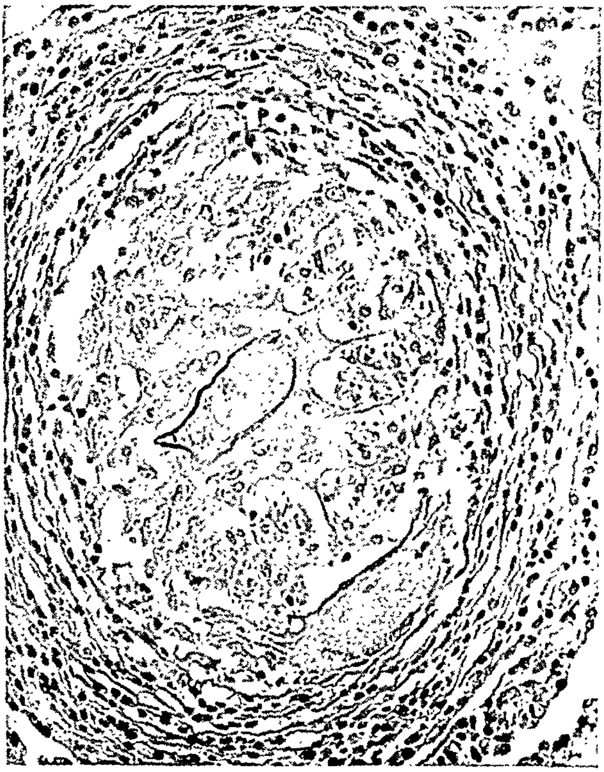

Fig. 3 (case 2).—Photomicrograph of lung biopsy specimen showing ovum of S. mansoni within giant cell.

Chest roentgenograms had a diffuse mottled appearan with nodular densities measuring 2 to 3 mm. in diamet and a reticular pattern of increased lung markings (fig. 4 The over-all appearance was similar to that seen in silicos Between February and July the lesions seemed to becom more prominent. Miniature chest roentgenograms of 195 1954, and January, 1955, showed no definite lesions; how ever, in May, 1956, a portion of the right upper lobe w visible on films of the shoulder and these showed nodul infiltrates of the lung. Pulmonary function studies show vital capacity, 3,700 cc. or 85% of the predicted norm one-second vital capacity, 91.5% of the observed; and ma mum breathing capacity, 106.5 liters per minute or 80% the predicted normal. Electrocardiograms did not show e dence of pulmonary hypertension.

During his early course at this hospital he had seve episodes of respiratory distress during the night and auscult tion over the lungs revealed diffuse expiratory wheez These were promptly relieved by rectal administration aminophylline. After the diagnosis of pulmonary schisto miasis was established he received two courses of stiboph The first was begun on Aug. 6; and after 45 cc. was a ministered in doses of 5 cc. intramuscularly on altern days, he developed T-wave inversions on the electrocard gram and complained of general malaise. After a one-mon rest period he was given a second course of treatment c sisting of 50 cc. of stibophen which he tolerated with difficulty. Follow-up sputum and stool specimens were p sistently negative for ova of S. mansoni. The chest roentge grams had not shown improvement when he was returned duty on Oct. 24. On follow-up in April, 1958, he complai of shortness of breath, tiredness, and chest pain, but additional information is available.

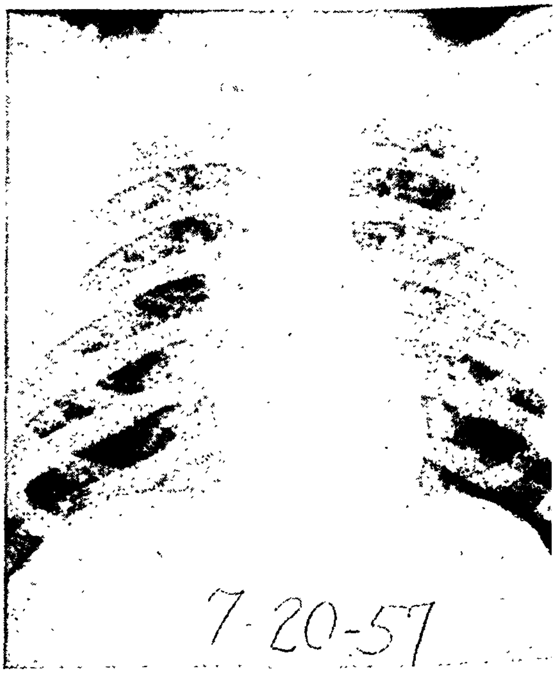

Fig. 4 (case 2).—Chest roentgenogram showing diff mottling.

Pathogenesis

There are three species of schistosomes (blood flukes) which commonly infect man. They are S. haematobium, which is found in the Middle East and Africa; S. mansoni, which was originally indigenous to Africa but was spread to the West Indies and South America during the slave trade; and S. japonicum, which is found only in the Far East. The schistosomes have similar life cycles but they differ in the organs to which they migrate and in the size and shape of the ova. Schistosomiasis, also known as bilharziasis, is so common in many areas of the world that it is estimated that approximately 5% of the world's population is infected.

The life cycle of the schistosomes involves man and various animals as reservoirs and specific species of snails as intermediate hosts. The ova pass from man in the urine or feces and hatch in water, liberating a free-swimming miracidium. The miracidia must penetrate the proper species of snail where two generations of sporocysts develop before the fork-tailed cercariae emerge. The cercariae swim about vigorously and easily penetrate the skin of persons washing, bathing, or wading in infected water. Infection can also take place by ingestion of cercariae. Penetration is aided by the lytic action of enzymes. The tail detaches and the larva is carried through the veins into the right heart, through the lungs, and into the systemic circulation. The passage through the pulmonary capillaries requires approximately three days and may be associated with transient signs and symptoms consisting of cough, rales, bronchopneumonia, sputum, fever, urticaria, and leukocytosis with eosinophilia.[2] Only those larvae survive that find their way to the intrahepatic portions of the portal vein, where they mature into male and female adult worms and then migrate against the blood stream to the organs of predilection; S. japonicum prefers the small intestine, S. haematobium the bladder, and S. mansoni the large intestine. The female of the pair deposits her eggs in the venules and, if she is not destroyed by the body defenses or by treatment, may continue to deposit eggs for as long as 20 years. In experimental infections in the hamster, the average number of eggs laid daily by a single worm was found to be 300 for S. mansoni and 3,500 for S. japonicum.[3] The ova become dislodged and may be disseminated to distant organs. Many are discharged into the portal circulation and become implanted in the liver where they often cause cirrhosis.

It has been postulated that the ova reach the lungs by way of the coronary vein and esophageal anastomoses or through the inferior hemorrhoidal plexus and the inferior vena cava. Experimental studies have shown that ova might reach the lungs by way of the vascular shunts in the liver.[4] A lymphatic route via the thoracic duct is a theoretical possibility since there are cases reported in which mesenteric lymph nodes contained many ova.[5] Once in the lungs the ova penetrate the arterioles and are quickly surrounded by inflammatory cells which eventually form pseudotubercles. These may be located in the adjacent interstitial tissue, respiratory bronchioles, or alveolar walls. In most cases the microscopic pseudotubercle will be the only pathological finding. In approximately 1 or 2% of all cases with pulmonary involvement there is extensive subacute and chronic granulomatous reaction sufficient to be detectable on chest roentgenograms. In addition to pseudotubercles there may be focal collections of histiocytes, eosinophils, chronic inflammatory cells, and fibroblasts. The arterioles may show acute and chronic angiitis. Angiomatoid formation is postulated to result from passage of ova through the arterial walls with focal destruction of the media. Shaw and Ghareeb [6] considered these to be pathognomonic of pulmonary schistosomiasis. Lopes de Faria [7] has pointed out how arteriovenous aneurysms may form and cause shunting of blood with clinical cyanosis.

Comment

Although scattered lung lesions are common in schistosomiasis, diffuse lesions such as have been described are not. In 1938, Shaw and Ghareeb,[6] from the Egyptian University, Cairo, published a detailed review of 282 autopsies on patients with schistosomiasis. They found that 95 (33%) had lung lesions which were divided as follows: 1. Parenchymatous tubercles only were found in 83 cases. 2. Focal arterial lesions appeared in 6. 3. Widespread arterial lesions producing the manifestations of Ayerza's disease were found in 6. In a study of 248 autopsies on patients with schistosomiasis, Martinez-Rivera and Koppisch [8] in Puerto Rico found that 161 (65%) had lung lesions, but in only three cases were the pulmonary lesions considered of clinical importance.

Chest roentgenograms may not always yield abnormal results, even though there are extensive lung lesions causing physiological abnormalities. This presents a difficult diagnostic problem, especially outside the endemic areas. The physiological abnormalities that occur in pulmonary schistosomiasis are (1) increased pulmonary vascular resistance and pulmonary hypertension, produced by diffuse obliterative endarteritis; (2) shunting of pulmonary artery blood as a result of extensive formation of arteriovenous anastomoses; and (3) restriction of ventilation produced by the fibrotic reaction in the lung. Both of the patients whose cases we have reported had restricted ventilation but little can be said about circulatory disturbances in their lungs since the critical physiological studies were not performed. The goal in their treatment was not to reverse the pathological changes but to prevent further extension of the disease.

Summary

Schistosomiasis may result in many serious complications and it is therefore desirable to survey individuals who come from endemic areas and to treat those who are infected. In patients coming from endemic areas, pulmonary schistosomiasis *should be included in the differential diagnosis of* scattered or diffuse infiltrative lesions of the lungs.

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FEVER OF OBSCURE ORIGIN—THE VALUE OF ABDOMINAL EXPLORATION IN DIAGNOSIS

REPORT OF SEVENTY CASES

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A study of the diagnostic value of laparotomy was made in 70 patients with febrile states that had lasted longer than two weeks and had been explained by repeated thorough physical and laboratory examinations. In 21 patients exploration of the abdominal cavity revealed malignant disease, and in 10 of these the lesion was a lymphoblastoma. In 15 patients evidence of specific infections was found, and in 5 of these it was tuberculous peritonitis. The surgical intervention entailed little risk. Its diagnostic value in cases of fever of obscure origin was evident.

Fever of obscure origin represents one of the most fascinating problems in differential diagnosis in the field of internal medicine. By fever of obscure origin we mean continuous fever of more than two weeks' duration or intermittent fever for a longer period for which a cause has not been found after careful, repeated interrogation, thorough, general physical examinations, and extensive laboratory studies. Such fever tests medical knowledge and diagnostic acumen to the utmost. The problem it presents has always been with us but seems to have assumed increased importance because of the availability of newer therapeutic agents, such as the antibiotics, cortisone, nitrogen mustard, and others.

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Many of the problems of obscure fever are the result of atypical clinical syndromes and variations of commonly known diseases; only rarely is a patient with such fever found to have an unusual disease.

We do not propose to discuss normal body temperature and the normal physiology involved in the regulation of body temperature. This can be found in any good physiology textbook and is summarized beautifully in the Croonian lecture of 1957 by Sir George Pickering.[1] Suffice it to say here that normal body temperature varies widely from person to person, and values up to 100 F (37.8 C) by mouth may be considered within normal limits in most people. When the temperature begins to be consistently more than 100 F by mouth, then one begins to think in terms of a febrile state and the possible cause for it. In some patients with anxiety-tension states the temperature may occasionally be slightly more than 100 F—as high as 101 F (38.3 C) and occasionally even higher—in the absence of any recognizable organic disease.[2]

Many good reviews of fever of obscure origin have appeared recently, including the volume by Keefer and Leard.[3] Other important reviews are those of Hamman and Wainwright,[4] Beeson,[5] Bennett,[6] Albrecht,[7] and Böttiger.[8]

Most observers have classified obscure fevers according to broad groups, as Beeson[5] has done: (1) infections of either localized or systemic variety, (2) malignant diseases, (3) collagen diseases, and (4) a miscellaneous group. An alternative and perhaps a more helpful way is to classify obscure fevers by body systems. Such a classification has the advantage of being an aid in differential diagnosis as one carefully questions the patient for possible clues which might lead to a diagnosis. Several such classifications have appeared.[9] In questioning the patient, we like to start at the top, with the central nervous system, and work down.

Our interest in obscure fever was aroused several years ago when we began to observe a number of patients with such fever in whom a definitive diagnosis could not be established when they were dismissed from the clinic. Among our colleagues and ourselves there was no unanimity of opinion regarding the value of exploratory laparotomy in patients with fever of unknown origin. Many were actually opposed to laparotomy in these patients when there were no signs or symptoms referable to the abdomen. We then decided to advise exploratory laparotomy in patients with obscure fever after a thorough clinical investigation revealed no diagnosis and yet indicated that the patient might have organic disease as the basis for the fever. Here we shall report our observations in 70 such cases.

Materials and Methods

All 70 patients were given thorough, detailed, repeated interviews for purposes of obtaining clues to the diagnosis, thorough repeated general physical examinations, numerous laboratory tests and x-ray examinations, biopsies as indicated, and, in selected instances, therapeutic trials with antibiotic or chemotherapeutic agents. Peritoneoscopy was not performed. These patients had febrile states of longer than three weeks' duration, and the cause of the fever could not be determined by any of the foregoing procedures. They represented patients seen personally and recently by us, patients seen and recalled by our colleagues, and other cases recorded in the files of the Mayo Clinic. Forty-one were males, and 29 were females. They ranged in age from 1 to 71 years, the average being 48 (51 years if the five patients in the pediatric age group, under 16, are excluded).

Microbiological procedures used included routine cultures for the common aerobes and anaerobes with use of fresh-meat-infusion blood agar, brain broth, and thioglycollate broth; cultures for Brucella; cultures for acid-fast bacilli with incubation at 37 and 32 C; cultures for fungi with use of mediums and techniques known to be useful for all the deep mycotic organisms; cultures for Leptospira; and inoculation of mice to detect Toxoplasma. When indicated, cultures were also made for Leishmania and Trypanosoma. In all cases material was examined directly with the aid of acid-fast stain, Wright's stain, and dark-field illumination. In most cases multiple specimens of tissue were examined in addition to the usual materials of blood, spinal fluid, sputum, urine, and stools. In a few cases special studies for viruses and rickettsias were made by complement-fixation test, inoculation of animals, or tissue culture.

In 30 of the 70 patients, there were no subjective symptoms or objective findings referable to the abdomen. Of the other 40 patients, 15 had subjective complaints and 34 had objective findings, 9 of the 40 having both. The subjective complaints referable to the abdomen consisted of tenderness, either localized or diffuse, and vague soreness, vague distress, actual aching, or other types of pain. Among the objective findings was enlargement of the liver, present in nine cases, in two of which the liver was also tender; it was palpable or questionably palpable in an additional 12 patients, in 2 of whom it seemed to be tender also. The spleen was palpable and enlarged in 19 patients; in one of these patients the enlargement was observed only on x-ray examination of the stomach. Ascites was present in one. There was a suggestion of an adnexal mass in one patient and an actual adnexal mass in another. There was splinting of the muscle of the left flank in one patient. These complaints and findings were not of diagnostic value.

The results are given in the table and are presented here by group: malignant disease, 21 patients; specific infections, 15; indeterminate disease, 14; entirely negative findings, 14; and miscellaneous diagnoses, 6. Of the 14 patients with entirely negative results on exploration, 8 had no signs or symptoms referable to the abdomen and 6 had signs or symptoms or both.

Results of Exploratory Laparotomy in Seventy Patients with Fever of Obscure Origin

Group	Condition	No. of Cases
1	Malignant disease (21 patients)	
	Lymphoblastoma	10
	Cancer, pancreas	5
	Cancer, kidney	2
	Cancer, sigmoid colon	1
	Cancer, gallbladder	1
	Hepatoma	1
	Retroperitoneal malignant lesion (from heterotopic adrenal tissue?)	1
2	Specific infections (15 patients)	
	Tuberculous peritonitis	5
	Histoplasmosis*	2
	Brucellosis of spleen (Brucella suis, 1) and of spleen and liver (1†)	2
	Abscess of liver (Staphylococcus pyogenes var. aureus)	2
	Viral hepatitis	1
	Granulomatous hepatitis (gram-negative bacillus)	1
	Streptococcus mitis bacteremia without clinical endocarditis	1
	Pyogenic abscess of spleen (Str. mitis)	1
3	Indeterminate disease (14 patients)	
	Granulomatous disease of undetermined cause (8 patients)	
	Granulomatous lymphadenitis	3‡
	Granulomatous abscesses of liver and hepatitis	3
	Granulomas of liver and regional lymph nodes	1
	Granulomatous disease of liver and bone marrow	1
	Nonspecific inflammation of lymph nodes and liver	5§
	Pyelonephritis?	1
4	Entirely negative results (14 patients)	
	Now well, no diagnosis at any time	8
	Died without diagnosis, no autopsy	2
	Rheumatoid arthritis	2
	Henoch's purpura	1
	Collagen disease?	1
5	Miscellaneous diagnoses (6 patients)	
	Thrombosis and thrombophlebitis of mesenteric veins and venules	1
	Periarteritis nodosa	1
	Endometriosis	1
	Common-duct stone (1); chronic cholecystitis and lithiasis (1)	2
	Intestinal lipodystrophy	1
	Total	70

* One case previously reported by Broders and co-workers.[11]

† Previously reported by Osmundson and co-workers.[12]

‡ In one patient biopsy of lymph node in home community at time of initial abdominal exploration and cholecystectomy revealed noncaseating granulomas. Exploration at Mayo Clinic showed only nonspecific inflammation in some enlarged para-aortic nodes.

§ One patient had leukocyte counts of 13,000-17,000 per cubic millimeter and microabscess in bone marrow, as well as enlarged para-aortic nodes and enlarged spleen.

Malignant Disease

In the 10 patients with lymphoblastoma no adenopathy was observed. The spleen was palpable in seven patients, and the liver apparently was enlarged and tender clinically in only one case. There was nothing from the clinical examination that could have led to a diagnosis. In two patients the fever was cyclic, in one for 1½ years and in the other for 11 years. In the latter patient a diagnosis of cyclic or "periodic" fever had been made until laparotomy, 11 years after the onset, revealed Hodgkin's disease. In seven patients the fever was continuous, occurring daily but of an irregular, remittent character.

The two patients with carcinoma of the kidney presented unusual diagnostic problems. One had two explorations before the diagnosis was made. Review of the excretory urograms indicated in retrospect that a diagnosis of malignant disease perhaps could have been entertained before the first surgical exploration. Despite this, the results of thorough exploration at the time of the first operation were negative. The other patient, who had had low-grade fever for six months, had normal-appearing excretory urograms and right retrograde urograms. He declined to have exploratory laparotomy. Three months later, laminographic examination of the left renal region elsewhere revealed a possible renal lesion; exploration disclosed renal carcinoma.

Four patients with cancer of the head of the pancreas had extensive metastasis to the liver. Two of these patients had mild soreness and pain in the right upper quadrant. The liver was not enlarged in any of them but was just palpable in one. In one patient exploration revealed a large amount of bile in the peritoneal cavity, and bile peritonitis. The superior border of the liver contained many nodules. One nodule in the dome of the liver was adherent to the diaphragm and apparently had ruptured, with the liberation of bile. Biopsy of this lesion revealed grade-3 squamous cell carcinoma which, the surgeon thought, probably arose from the gallbladder. However, subsequent postmortem examination revealed that the primary lesion was in the pancreas.

The patient with malignant disease of the sigmoid colon underwent abdominal exploration because of the finding of asymptomatic cholelithiasis. She had had no symptoms or signs that were referable to the abdomen or the gastrointestinal tract. She had had fever cyclically for about seven years, but six months before she came to the clinic the fever had become almost continuous. Exploration of the abdomen at the time of cholecystectomy revealed an inflammatory mass in the sigmoid. A second surgical exploration subsequent to suitable preparation of the intestine revealed a polypoid, grade-1 adenocarcinoma extending through the muscle and serosa to involve the pericolonic fat; the sigmoid was resected. No lymph nodes were involved. Proctoscopic examination and x-ray examination of the colon had not been done. The patient was completely well after three years and had had no fever. Two other patients with a malignant lesion of the sigmoid associated with prolonged fever have been seen, one with extensive metastasis to the liver which was not evident before exploration and the other without metastasis. Proctoscopic examinations in both patients revealed annular and ulcerative lesions in the absence of any other findings. These two patients are mentioned because it could not be determined without laparotomy whether other causes for the obscure fever were present, but they are excluded from the series because of diagnosis by proctoscopy. Malignant disease of the sigmoid alone has been associated with fever of unknown origin, and similar cases have been described in the literature.[10]

In the patient with hepatoma the liver was irregular, nodular, firm, and tender and was felt about 8 fingerbreadths below the right costal margin. The patient's temperature ranged up to 103 F (39.4 C), and he had chills and vague, recurring pain in the upper part of the abdomen. The diagnosis was made at surgical exploration and confirmed at postmortem examination.

The patient with retroperitoneal malignant neoplasm had had an irregular daily temperature ranging up to 101 F (38.3 C), together with malaise, weariness, fatigue, and night sweats for four months. The examination revealed only some enlarged axillary lymph nodes on the left. Biopsy of these revealed only "hyperplastic" nodes; the cultures gave negative findings. The only positive laboratory findings were increased sedimentation rate (109 mm. per hour by the Westergren method), marked rouleau formation on the blood smear, and a positive skin reaction to the tuberculin (purified protein derivative) test. All other tests and examinations gave negative results. Exploratory laparotomy disclosed only a cluster of enlarged firm lymph nodes at the ligament of Treitz, situated on the aorta and vena cava. No primary source of the neoplasm could be found. Biopsy revealed a grade-4, clear-cell, malignant lesion which, it was thought, might have arisen from heterotopic adrenal tissue.

Specific Infections

In patients with tuberculous peritonitis the abdomen can appear to be almost normal on physical examination despite the extent of the disease that is found in it. In three of five cases physical examination of the abdomen gave negative results; there was no evidence of fluid. In the fourth case moderate ascites was present. This patient had had splenectomy in his home community for what was thought to be thrombocytopenic purpura. Granulomatous lesions had been seen at the time of exploration, and it had been thought that a fungous disease was the cause of the difficulty. Reexploration of the abdomen with biopsy at the clinic after it had not been possible to make a diagnosis revealed tuberculosis when acid-fast bacilli were found in smear and culture. In the fifth case abdominal examination revealed some tenderness in the right lower quadrant and the sensation of a mass in the left side of the pelvis. In the four patients on whom tuberculin skin tests were performed the reaction was positive. In all five cases the diagnosis was proved bacteriologically.

In two patients a definite diagnosis of histoplasmosis was made at the time of exploration. In one, exploration was performed for diagnosis because it was thought that hepatic disease was the basis for the fever. Biopsy of the liver at the time of laparotomy revealed Histoplasma capsulatum. Postmortem examination elsewhere revealed histoplasmosis of the heart valves also. Clinically, the patient had presented some features of bacterial endocarditis, but the results of blood culture were negative. This case has been reported previously.[11] The second patient had recurring chills and fever, malaise, weakness, loss of weight, sweats, and an enlargement of the spleen together with pancytopenia over a period of six months. Abdominal exploration and splenectomy were performed in an attempt to make a diagnosis. H. capsulatum was cultured from the noncaseous granulomatous lesions of the spleen and liver.

One of the two patients with brucellosis had had periodic fever of 17 years' duration resulting from Brucella suis infection of the spleen. This case will be reported separately. Cure followed splenectomy and combined antibiotic therapy with tetracycline and streptomycin. The other patient with brucellosis had had fever each summer for 14 years; this case has been reported previously.[12] Brucellosis was suspected when needle biopsy of the liver revealed granulomas; cultures of the granulomas were negative for B. suis. The Brucella agglutination titer was then found to be 1:800. A combination of tetracycline and streptomycin had been given for two weeks when exploratory laparotomy became necessary because of moderately severe pain in the left upper part of the abdomen. Only then was a diagnosis of brucellosis established by culture.

In one of the two patients with hepatic abscess the liver was (questionably) slightly enlarged, and tender. The patient who had hepatitis without jaundice was a surgeon who was most anxious to know the cause of his fever.

The patient with granulomatous hepatitis was a 1-year-old who had been ill for about six months with irregularly occurring fever, chills, anemia, thrombocytopenia, hepatomegaly, and splenomegaly. Much antibiotic therapy given at home had apparently not been helpful. The temperature after admission to the clinic had been irregular, going as high as 105.4 F (40.9 C), and fever had been present continuously for two weeks. Cultures of the blood, urine, and stools gave negative results. It was thought that exploration would be the best method to settle the diagnostic doubt. At exploration the spleen was found to be four times normal size; the liver was enlarged, and histopathologically it was the site of "granulomatous hepatitis." There were no enlarged retroperitoneal nodes. No discrete abscesses or granulomas were seen. Cultures for B. suis, acid-fast bacilli, and fungi gave negative results. However, an unidentified gram-negative bacillus, not a recognizable pathogen, was isolated. The patient died suddenly two days after operation. One can only speculate on whether the gram-negative bacillus was causative or a contaminant.

The patient who had Streptococcus mitis bacteremia without clinical evidence of endocarditis underwent abdominal exploration because no diagnosis could be made clinically even though one of the many blood cultures showed Str. mitis. He was having recurrent daily chills and fever. He had had cholecystic disease and had undergone cholecystectomy previously and also surgical treatment for chronic relapsing pancreatitis. Clinically the liver was slightly enlarged and tender, and it was thought that the disease process causing the febrile state was probably located in the abdomen. At operation, exploration was difficult; nothing was found except many adhesions in the cholecystic bed and at sites of previous surgical treatment. Cultures obtained from these areas at exploration revealed Str. mitis. Appropriate therapy with penicillin and streptomycin for a two-week period was curative.

The patient with a Str. mitis splenic abscess which ruptured retroperitoneally had had five episodes of fever (temperature up to 103.4 F [39.5 C]) and chills lasting two to five days over a period of two or more months. It was thought that a good response to antibiotics had occurred with each attack. The patient had had intermittent pain in the left upper abdominal quadrant for more than eight years; during the same two months of the febrile episodes, the distress had been more pronounced and he had some characteristics of pleuritic pain. There had also been anorexia and a loss of about 20 lb. (9.1 kg.). Study of the patient in his home community had revealed no abnormalities. Examination at the clinic disclosed only a slightly palpable liver and some tenderness in the left upper quadrant of the abdomen. Positive laboratory findings were as follows: sedimentation rate, 120 mm. in one hour; hemoglobin level, 11.7 Gm. per 100 cc. of blood; and moderate rouleau formation on the blood smear. The left hemidiaphragm was slightly elevated. X-ray examination of the entire gastrointestinal tract and kidneys gave negative results. All other tests also were not helpful. Exploratory laparotomy revealed a mass of induration across the upper part of the abdomen in the retroperitoneal region. An abscess of the spleen had perforated retroperitoneally, and the infection had extended up under the tail of the pancreas, across the midline; splenectomy was performed. The other structures were normal. Cultures revealed only green-producing streptococci sensitive to less than 0.05 unit of penicillin per cubic centimeter. Postoperative antibiotic therapy with penicillin brought rapid improvement and cure.

Indeterminate Disease

The patients in group 3 had nonspecific findings on exploration. In the eight patients with unidentified granulomatous disease (granulomatous lymphadenitis, hepatitis, hepatic abscesses, or disease of the bone marrow), the liver was enlarged slightly in three and the spleen was palpable and enlarged in two at the time of physical examination. All cultures from multiple biopsy specimens of involved tissues removed at operation were negative for acid-fast bacilli, Brucella, fungi, and other bacterial pathogens. Noncaseating granulomatous lesions were noted in six of these eight patients and caseation in two. One of the last two patients had had two laparotomies, one in Hawaii and one at our clinic. The findings in the liver were the same, and the cultures were negative for any pathogens on both occasions; the liver was studded with many abscesses containing granular, thick, greenish-yellow material. In six of the eight patients the febrile episodes disappeared and the patients have remained well; the other two died. One of the deaths was that of a 3-year-old boy in whom a diagnosis of granulomatous hepatitis and abscess was made at laparotomy. Febrile episodes continued until death occurred 16 months after operation. The patient had many of the features of the entity described by Berendes and co-workers[13] as "fatal granulomatosis of children." The other death, that of a 50-year-old man, was attributed to an increasingly severe pancytopenia and a hypocellular condition of the bone marrow resulting from a marked granulomatous reaction of the marrow. The cause of the latter was obscure.

In six patients with nonspecific inflammatory disease, a definitive diagnosis could not be made from abdominal exploration. One patient had a mesenteric lymph node removed at home. The histological section reviewed by a clinic pathologist was reported as showing noncaseating granuloma "consistent with sarcoid." The nodes had been removed at the time of cholecystectomy. Laparotomy at our clinic revealed a spleen that was three times normal size, a para-aortic node 1 cm. in diameter, and some mesenteric nodes that were thought not to be abnormal. Biopsies of the liver and the rectus muscle gave negative results. The para-aortic node showed "inflammation" and the mesenteric nodes showed "reticulum hyperplasia." All cultures gave negative results. Follow-up examination three months later showed the patient to be improving, gaining weight, and afebrile.

In a second patient abdominal exploration gave negative results except for many creamy-white, raised, glistening, punctate nodules 2 mm. in diameter on the liver and spleen. The pathologists reported "normal liver except for focal subcapsular accumulations of lymphocytes." All cultures gave negative results. Biopsies of axillary lymph nodes, rectus muscle, and the appendix also gave negative results. The fever subsided postoperatively.

A third patient had only some slightly enlarged nodes in the mesentery of the small intestine and in the periaortic region; also, a node that measured 2 by 1.5 by 0.7 cm. was present retroperitoneally above the head of the pancreas. The spleen was two and one-half times normal size. All cultures of the nodes and other tissues gave negative results. Histopathological examination of the nodes revealed "inflammatory reaction with hemosiderosis" of doubtful cause. Sections of a node that had been removed in the patient's home community showed "rather marked reticuloendothelial hyperplasia." The patient was well five years later.

A fourth patient had only slight enlargement and mottling of the liver with focal collections of polymorphonuclear leukocytes and lymphocytes in the liver. These were thought to be nonspecific findings. No other intra-abdominal abnormality was noted. Postoperatively 20 mg. of prednisone (Meticorten) given daily for three weeks curbed the increase in temperature somewhat. However, low-grade fever, weakness, anorexia, and deterioration persisted. All cultures for pathogens had given negative results. After dismissal of the patient, his condition deteriorated further and he died at home about four months later. Unfortunately, autopsy was not performed, and the cause of the fever remained indeterminate.

A fifth patient had what appeared to be an ulcerating lesion of the lower pole of the left kidney, as revealed by excretory and retrograde urograms; a lower calyceal deformity was also evident. Abdominal exploration gave negative results; the left kidney was felt to be normal. The lower one-third of this kidney was resected. Histopathological examination revealed only mild inflammatory clusters of lymphocytes and foci of calcification. The urologist thought that these minimal pyelonephritic changes were not sufficient to account for the fever (102 to 104 F [38.9 to 40 C]), sweats, and occasional chills that had been experienced for two months preoperatively. The patient's condition improved, and the episodes of fever diminished postoperatively and eventually disappeared. Cultures of the urine had revealed Aerobacter aerogenes; cultures of the excised renal tissue gave negative results for bacterial pathogens.

The sixth patient had two laparotomies at the clinic. The first was in 1948, at which time cholecystectomy was done; the liver was large and boggy, and a moderate hepatitis was evident. The gallbladder contained a large solitary stone. The pancreas was firm and slightly enlarged. The spleen was two times normal size. Histologically, nests of inflammatory cells were observed along the liver cords. Cultures gave negative results. The second exploratory laparotomy, performed in 1952, revealed only mild fibrous pericholangitis. The condition of the liver was improved, and the spleen was smaller. The patient continued to have recurring bouts of fever with severe anorexia every three or four months which lasted 7 to 10 days; he continued to lose weight and had recurring bouts of abdominal pain. His condition had deteriorated when he was last seen at the clinic in 1955. He looked emaciated and was thought to have some pathological change in the right side of the abdomen. He refused further tests and further exploration. Three months later the home physician found a large mass in the right lower quadrant which seemed to fill the entire pelvis. Incision and drainage revealed much pus; culture at home gave negative results. The patient permitted no other studies by the home physician. His condition continued to deteriorate. The diagnosis has remained indeterminate.

Entirely Negative Results

In group 4 (14 patients), abdominal exploration did not reveal any disease or abnormality. Eight of the patients are now well, and in them no diagnosis has ever been made. One of these patients, however, was suspected of having histoplasmosis; a single episode of persistent low-grade fever had been present for six weeks. Abdominal exploration gave completely negative results. The skin reaction had been positive for histoplasmosis. Two months after surgical exploration the patient was well and afebrile; miliary nodules were seen at the bases of both lungs. A presumptive diagnosis of histoplasmosis was made. However, the diagnosis was not proved.

Two patients died at home, possibly from malignant disease; however, postmortem examinations were not made. In two patients—a 4-year-old boy and a 20-year-old woman—signs and symptoms of rheumatoid arthritis finally developed. In one patient, Henoch's purpura was finally diagnosed. One patient became afebrile with postoperative cortisone therapy; review of the entire clinical problem suggested a diagnosis of collagen disease.

Miscellaneous Diagnoses

The patient with thrombophlebitis of the mesenteric veins and venules had had intermittent fever for about six weeks. She was dismissed from the hospital after thorough study and when the temperature had become normal. That same evening abdominal pain developed; she was readmitted to the hospital and subjected to exploratory laparotomy.

The patient with the diagnosis of periarteritis nodosa was studied thoroughly at the clinic and underwent abdominal exploration in the home community. Extensive examinations at our clinic had revealed only chronic cholecystitis with cholelithiasis.

The patient with endometriosis had had brucellosis six years before the onset of her fever. She had a small adnexal mass. The Brucella agglutination titer was 1:200. It was felt that a Brucella abscess might be present. Exploration revealed only endometriosis. The patient had not had any previous estrogen therapy or surgical treatment.

The patient with choledocholithiasis had been referred to the clinic with the diagnosis of probable bacterial endocarditis. Fever had been present for seven weeks at home, and it continued here. Extensive study resulted in suggestions of many other diagnoses. Details of the history were difficult to obtain. The patient had recurrent febrile episodes with chills, night sweats, undocumented jaundice (one episode), anorexia, and vague pain in the right upper part of the abdomen; these episodes on occasion were suggestive of biliary colic. Examination revealed severe tachycardia, an enlarged rheumatic heart with mitral stenosis and atrial fibrillation, and, eventually, a palpable, distended gallbladder. The positive laboratory results were increased sedimentation rate (110 mm. in one hour), anemia with eosinophilia and marked rouleau formation evident on the blood smear, and grade-3 retention of dye with the sulfobromophthalein test of hepatic function. Many blood cultures gave negative results. Needle biopsy of the liver revealed cirrhosis. Laparotomy disclosed distention of the gallbladder and enlargement of the liver and spleen. The common duct was greatly dilated—so much so that the surgeon thought that a choledochal cyst was present. A single stone, 1.3 cm. in diameter, was found. Choledochoduodenostomy, removal of the stone, and biopsy of the liver were performed. The remainder of the abdominal exploration gave negative results. Histopathological examination of sections from the liver revealed periportal infiltration with neutrophils and lymphocytes. Postoperatively the patient became afebrile.

The patient with cholecystitis and cholelithiasis had had intermittent febrile episodes with chills, malaise, arthralgias, and sweat lasting about 24 hours, the fever itself being present during only four to six hours of the entire episode. There were no symptoms referable to the gastrointestinal system and no history of jaundice. The only abnormal laboratory findings consisted of slightly increased serum bilirubin level (0.5 mg. per 100 cc. direct and 0.7 mg. indirect) and a sulfobromophthalein retention of 8%. The cholecystogram was interpreted as showing a normally functioning gallbladder. At exploration, subacute gangrenous cholecystitis with cholelithiasis was found. The gallbladder was tense, edematous, and gangrenous. It was amazing that the patient had no symptoms referable to the right upper part of the abdomen.

The patient with intestinal lipodystrophy (Whipple's disease) was a 44-year-old man with a history of periodic fever for three and one-half years; initially, for a 16-month period, the three-to-four-day periods of fever, chills, sweats, malaise, and arthralgias occurred at monthly intervals. The patient said they took place "almost like clockwork." Then the febrile episodes recurred with gradually decreasing time intervals until just prior to admission, when they recurred every three to four days. The patient had constipation with the episodes, but otherwise had no significant gastrointestinal symptoms. At no time did he have diarrhea. Loss of weight occurred only during the last year of symptoms prior to laparotomy. Almost from the beginning, the patient had been given steroids as long as the symptoms lasted during the febrile episode. The examination gave entirely negative results. The only abnormal laboratory findings prior to operation were increased sedimentation rate (88 mm. per hour by the Westergren method), mild anemia, and slight leukocytosis. At operation, the spleen was found to be about twice normal size and mesenteric lymph nodes were enlarged. Biopsies of these nodes and of the jejunum revealed the typical findings of intestinal lipodystrophy.

Comment

We believe that exploratory laparotomy should be considered seriously in selected patients when thorough and repeated studies do not reveal the cause of an indeterminate fever. If a thorough, detailed history and physical examination reveal no helpful leads or positive findings, if all of the laboratory tests give no clues, if tissue cannot be obtained for study and diagnosis, and if the patient continues to look chronically ill and has a history of loss of weight, some anemia, and a high sedimentation rate, then one should think seriously of abdominal exploration. The basis for our advocacy of this procedure is the fact that the abdominal cavity and the retroperitoneal region cannot be examined adequately or visualized thoroughly with the available diagnostic procedures except by exploration. This is in contrast to other body systems, such as the central nervous system, the respiratory tract, or the genitourinary tract, where fairly precise examination and visualization are possible, so that one may say with some assurance whether disease is present as a basis for the obscure fever. Exploratory laparotomy should be considered as one of the steps in a planned study of selected patients with obscure fever.

In the selection of patients, care should be used to exclude those who have had the uncommon clinical syndrome of "periodic fever"[14] over a long period. In this syndrome the patient has febrile episodes that occur at intervals ranging from two days to six months, but usually from 7 to 28 days. Once the cycle has been set it generally remains the same. The episodes may recur for as long as 30 to 40 years and they may last for 12 hours to 10 days. The temperature may go as high as 105 F (40.5 C) and is usually accompanied by the systemic symptoms that go with episodes of high fever. The leukocyte count may be normal or increased. The sedimentation rate may be slightly increased with the attacks but is normal between attacks. These people have good health between attacks and manifest no loss of weight or anemia. They look well and have no other evidence of organic disease.

If abdominal exploration, perhaps as the last of a planned series of diagnostic procedures, does not reveal a diagnosis, then we will have done everything for the patient that it is possible to do. Therapeutic trials can be given subsequently with antibiotics or with other chemotherapeutic agents, or the patient can be sent home for further observation. Until abdominal exploration is done in these patients, we feel that all manner of therapy should be withheld except in certain selected patients who, one suspects, should have an adequate trial of antibiotic therapy first to see if some hidden infection can be brought under control.

Therapeutic trials are indicated in situations in which it is felt that a specific infection or specific disease entity is present. They are justified when repeated examinations have not led to a diagnosis and the patient's condition continues to deteriorate. One should be careful in the interpretation of the response that is obtained with a therapeutic trial. Bennett[6] has stated that a nonspecific response coincident with the administration of a drug can be very misleading. This has been our experience also. One should try to obtain unequivocal evidence of a diagnosis by tissue examination or cultures if at all possible before any therapy is given. Exploratory laparotomy should precede antibiotic or other drug therapy, if possible, in patients who are suspected of having organic disease. Bennett[6] has cited two excellent examples in which tuberculous peritonitis was felt to be present. In both instances other diagnoses resulted; autopsy revealed lymphosarcoma in one, and abdominal exploration showed cancer of the colon with perforation and localized abscess formation in the other.

Therapeutic trials should be carefully planned and carried out, and the results should be interpreted with caution. We have seen one patient with obscure fever in whom we could not make a diagnosis and who had a definite heart murmur which was thought to be of organic origin. Many consultants felt that the patient had endocarditis, and he was given a therapeutic trial with antibiotics. The temperature did not come down to normal during treatment with penicillin and streptomycin but did so on the 10th day after tetracycline was added to the therapeutic program. At postmortem examination a miliary granulomatous type of Hodgkin's disease was found in the liver, spleen, and some of the other abdominal viscera. The patient did have organic heart disease, but it was a congenital perforation of one of the mitral valve leaflets and was uncomplicated by any infection.

A recent review of treatment of pulmonary and pelvic tuberculosis at the Johns Hopkins Hospital indicated that treatment with either isoniazid or streptomycin and aminosalicylic acid causes lessening of fever in 80% of the patients within six days[6]; more than 95% responded by the third week, and it was concluded that treatment for one month constitutes a trial of therapy with antituberculosis drugs.

Our own experience with bacterial endocarditis in patients who present a rather typical clinical picture, except that organisms have not been cultured from the blood, is that the therapeutic re- [redacted] n of 10 [redacted] Gm. of [redacted] Gm. of [redacted] to 7 days and [redacted] orough trial of [redacted] bacterial endo- [redacted] include tetracycline [redacted] cover for possible gram-negative bacterial infections. If no response is obtained in five to seven days with penicillin and streptomycin, 3 Gm. of tetracycline in divided dosage should be added to the program for another three to five days. Failure of the temperature to come down with this regimen of [redacted] 10 [redacted] obscure fever in most instances.

Clinical reviews of fever of unknown origin give only passing mention to the value of laparotomy in patients with indeterminate fever.[16] Hand,[17] in a recent review of unexplained fever, stated, "More and more, we are resorting to abdominal exploration or diagnostic thoracotomy when other measures fail." This has been our practice also.

All patients with obscure fever should have x-ray [redacted]. When [redacted] und on x-ray examination, cholecystectomy should be carried out and the rest of the abdomen and the retroperitoneal region should be thoroughly investigated. Most observers would agree about this. There is some question, however, in the minds of many clinicians whether exploratory laparotomy should be performed when examination and investigation of the patient repeatedly give negative results. Some think the procedure is too radical; others prefer treatment with nitrogen mustard, x-rays, or cortisone in the hope that improvement will occur; and still others prefer continued observation and repeated investigation until the cause of the fever becomes obvious. However, when a patient has been ill for some time with obscure fever and comes to the physician with the hope that something may be found and his symptoms relieved, he should be advised to undergo exploration after thorough study if it is still thought that organic disease is present. These patients should not be treated with x-rays or nitrogen mustard before a definitive diagnosis has been made; such nonspecific treatment only serves to confuse the clinical picture further. The fact that a febrile reaction ceases after x-ray therapy or nitrogen-mustard therapy is not proof that the patient had a lymphoblastoma or some other lesion.

In approximately 80% of our series of 70 patients, something was found at operation. In 60% a definite diagnosis was made; in an additional 20% the disease was of a nonspecific granulomatous nature or it was a nonspecific infection; and in approximately 20% nothing was found.

In none of the eight patients with nonspecific granulomatous disease was there a history of allergy. Eosinophilia was noted in only one; that was the patient with caseating granulomatous abscess who had had two laparotomies. The granulomatous lesions apparently were limited to the abdomen only. Seven of the eight patients were well at the time of writing. The histological appearance of the biopsy specimen in several patients was consistent with a diagnosis of "sarcoidosis."

It was impossible to know the cause of the granulomatous disease in these eight patients. They could be presumed to have had benign, perhaps inflammatory, disease of some kind. However, the consistency with which all cultures gave negative results would tend to exclude bacterial infection, although previous antibiotic therapy in some of these patients may have rendered the cultures negative. The patient with the caseating granulomatous abscesses in the liver had a high eosinophil count. She had taken 1.25 mg. of conjugated estrogenic substances (Premarin) daily for years, and it was considered possible that this drug might have been antigenic in this patient, giving rise to a hypersensitivity granulomatous type of reaction. She was advised to take no antibiotics or other medicament postoperatively. She recently wrote that her fever gradually disappeared over a period of six to eight months and that she is now well. It is quite possible that these eight patients represent instances of hypersensitivity granulomatosis.[18]

It should not be forgotten that infection and malignant disease of the kidneys may be present even when the urographic appearance is normal. An excretory urographic examination should be one of the earliest tests performed in patients with fever of obscure origin. At laparotomy the kidneys should actually be visualized, not merely palpated. This point is illustrated by one of the two patients with malignant disease of the kidney as a source of obscure fever. On the first abdominal exploration the kidneys felt normal on palpation; at the second exploration four months later, after further urologic study, the renal carcinoma was found. In the original 200 cases of Kark and co-workers[19] in which needle biopsy of the kidney was performed, there were 5 cases of bacterial renal infection in which cultures of the urine gave negative results. These five cases represented problems of obscure fever. Appropriate antibiotic therapy was curative after diagnosis resulted from needle biopsy of the kidney. This raises the question of doing a needle biopsy of the kidneys before or at the time of each laparotomy to be sure that renal infection does not exist.

Summary and Conclusions

An analysis of 70 recent Mayo Clinic patients who had fever of obscure origin and who underwent abdominal exploration for purposes of diagnosis indicates that this procedure should be carried out when a planned investigation of such patients does not reveal a diagnosis. Patients who have had repeated episodes of fever, who continue to manifest debility and chronic illness, and whose disease is progressive should be considered for exploratory laparotomy. Evidence of continuing loss of weight, a high sedimentation rate, and progressive anemia in the absence of a definitive diagnosis should aid in the decision for exploratory laparotomy.

The data presented indicate that in approximately 80% of such patients something will be found at the time of exploration and that a precise diagnosis will be made in about 60%. Patients who have had only one prolonged bout of fever and whose condition is improving despite the previous presence of anemia, increased sedimentation rate, and loss of weight should not be subjected to exploratory laparotomy.

In approximately 20% of our cases abdominal exploration revealed indeterminate granulomatous disease or nonspecific infection, and in about 20% it was completely unrevealing. The operative risk in these patients is minimal; the postoperative morbidity is slight. No deaths occurred in this series. Exploratory laparotomy is frequently of real diagnostic value in selected patients with fever of obscure origin.

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CONTROL OF INTRACTABLE PAIN IN ADVANCED CANCER BY SUBARACHNOID ALCOHOL BLOCK

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Relief from otherwise intractable pain in the lower portions of the body can frequently be afforded by the subarachnoid injection of absolute alcohol. The technique here described is believed to give more predictable results and to cause less of the distressing complications (paralyses, paresthesias, and vesical and intestinal dysfunction) than do older methods. This method, involving the careful positioning of the patient and other precautions to limit the action of the alcohol to the dorsal nerve roots, was applied in 106 patients with hopeless malignant disease. The results were classed as good in 53 and fair in 35. Ten spinal cords were examined at subsequent autopsies, and the most constant finding was demyelinization of the dorsal roots of the spinal nerves. The effects extended peripherally to the dorsal root ganglia and centrally into certain tracts within the cord. The abolition of pain was not always permanent, especially since metastases sometimes appeared in distant parts, but some patients were completely relieved for eight months or more.

In the constant search for a method to relieve intractable pain in advanced malignant disease, many agents have been used. This communication will present the clinical results of 175 subarachnoid alcohol segmental blocks, the histopathology of 10 spinal cords after this procedure was done, and a brief review of the neuroanatomy concerned.

The first report of the use of subarachnoid alcohol for pain relief was by Dogliotti [1] in 1930. Several other favorable reports [2] were published during the following several years, all concerned with the use of this technique in the treatment of intractable pain in malignant conditions. The majority of the injections were accomplished in the lumbar interspaces and more often than not resulted in rectal and bladder incontinence, motor paralysis of the lower extremities, and poor pain relief. The explanation of these unfortunate complications is that the nerves in the lumbar area are mixed nerves, carrying both sensory and motor impulses. Hence, if alcohol is introduced into this area, both modalities will be disturbed. Thus, the procedure described by Dogliotti never has gained widespread use or acceptance because of the unpredictability of its effects and the occurrence of distressing complications, that is, muscle paralyses, bladder and intestinal disturbances, and painful paresthesias.

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Neuroanatomy

A brief description of a typical spinal nerve [3] will show the anatomic basis for this procedure. Each spinal nerve is composed of two roots: an anterior (ventral, motor, efferent) and a posterior (dorsal, sensory, afferent). The posterior root is the larger of the two. It is composed of multiple rootlets which arise from the posterolateral sulcus of the spinal cord. These unite to form two bundles which join the spinal ganglion. After leaving the ganglion, the posterior root joins the anterior at the intervertebral foramen. Both anterior and posterior roots are covered by pia, arachnoid, and dura. The two roots pierce the dura separately, and each root receives an investment of this membrane which is continuous with the epineurium of the combined nerve (fig. 1).

The roots of the spinal nerves below the third cervical vertebra run obliquely downward and laterally. This downward angle increases progressively throughout the length of the cord so that at its termination at the interspace of L-1 and L-2 the roots are parallel to the long axis of the cord. It is therefore practical to interrupt the dorsal roots at their cord level rather than at their vertebral level (fig. 2). Most commonly the cord terminates at the body of the first lumbar vertebra, occasionally at the upper portion of the body of the second lumbar vertebra. For practical purposes, the L-1 and L-2 interspace is considered the level of termination. The dorsal roots are accessible for blockade at specified interspaces above the lumbar area only.

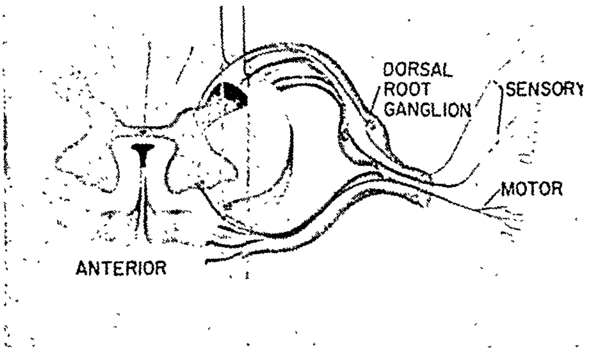

Fig. 1.—Diagram of typical spinal nerve.

The dorsal root fibers [4] subserving tactile, thermal, pain, and proprioceptive sensations enter into synaptic relations within the gray matter of the cord, not only with secondary sensory neurons which relay impulses toward the cerebral cortex but also with association and commissural neurons which are connected with motor neurons and are concerned with spinal reflexes. With this arrangement of ascending, descending, crossed, and uncrossed pathways, it is apparent that pain impulses may be appreciated by any one of several avenues of ingress at multiple segmental levels.

There are two ascending tracts of importance to this discussion: the lateral and ventral spinothalamic tracts. Briefly, these tracts are as follows:

In the ventral spinothalamic tract, the unipolar cell body of the first order neuron is in the spinal ganglion. At varying levels, synapses are made in the columna posterior with the second order neuron. The cell body of the second order neuron is in the posterior gray column. It sends an axon across the median plane to the ventral spinothalamic tract in the opposite anterior funiculus and thence to the thalamus. From the thalamus, axons of the third order neuron go by way of the thalamic radiation to the somatesthetic area of the cerebral cortex.

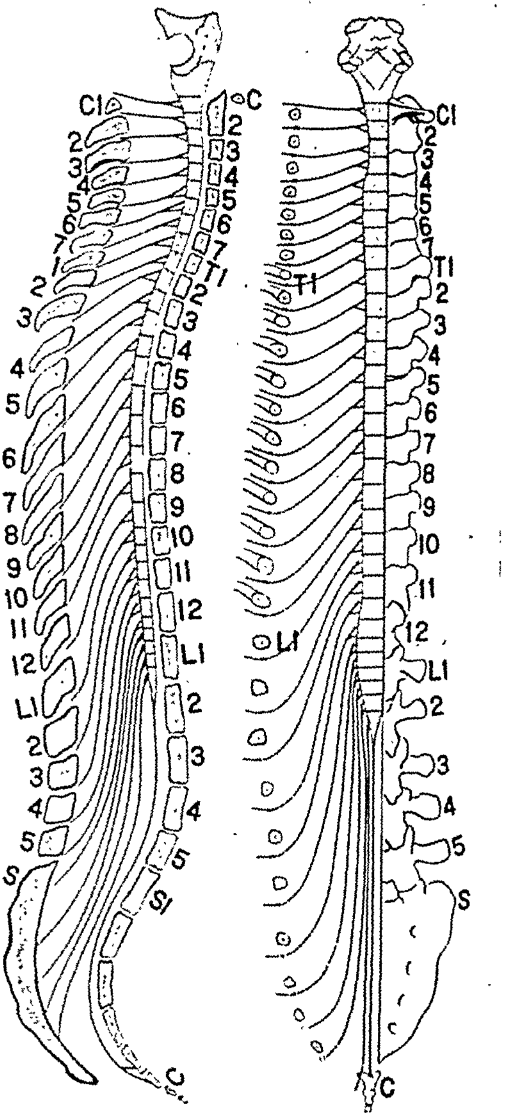

Fig. 2.—Roots of spinal nerves.

In the lateral spinothalamic tract, the unipolar cell body of the first order neuron is in the spinal ganglion and sends a process to the skin and to the deeper tissues. The central process immediately terminates in the cord. The second order neuron is located in the posterior gray column. The axon immediately crosses the medial plane and ascends in the lateral spinothalamic tract to end in the posterolateral ventral nucleus of the thalamus. From the posterolateral ventral nucleus of the thalamus, the third order neuron conveys thermal and painful impulses by way of the thalamic radiation to the somatesthetic area of the cerebral cortex.

Technique

The technique of subarachnoid alcohol block[5] is little different from that normally used for spinal anesthesia. The principal difference between the two is one of position of the patient. It is far preferable to use a standard operating table with its inherent mechanism for "flexing" the table. The patient must be placed on the table with the side to be blocked uppermost and the site of needle insertion directly over the "break" in the table. The table is then flexed so that the needle site is at the peak of the bend in the thoracic curve. That is, the head and hips are always lower than the site of injection. The body is then rotated anteriorly approximately 45 degrees. The patient is securely fastened in this position. If a bilateral block is desired, the patient is placed in the prone position with the peak of the curve made by the flexed table at the needle site as before. Each of these two positions brings the posterior roots to the highest point in the dural tube (fig. 3).

After the positioning, the subarachnoid puncture is made in the routine manner. One must be absolutely certain that the bevel of the spinal needle is lying freely within the subarachnoid space and not in the peridural space or the cord itself. It may be necessary to aspirate cerebrospinal fluid instead of waiting for it to appear at the hub of the needle, since, occasionally, when the patient is in the prone position the spinal fluid pressure is too low for free flow. The actual injection of the absolute alcohol must be slow and deliberate. The patient must be warned prior to injection that he may feel exquisite burning, warmth, or sharp pain in the segment involved. This sensation usually lasts a few seconds at peak intensity and then fades away during the next few minutes. The area of paresthesia indicates the segment blocked, of course, and is a good index of the level of blockade.

If there are multiple segments involved, it is more desirable to use two or three needles at successive interspaces than to inject a large volume of solution through one needle. If the latter is done, motor paralysis may result, since the large volume of alcohol may diffuse anteriorly to involve the anterior roots. After the alcohol has been injected, the patient must remain in the position for at least 45 minutes to allow the alcohol to become fixed to the neural tissue and to be diluted by the spinal fluid. The patient may then be turned to the supine position and returned to his bed, where he should remain flat for two hours.[5]

After the block, the evaluation of the degree of pain relief is a difficult task. The enthusiasm of the operator for the procedure may cause interpretation of more pain relief than is actually present. The best indexes of pain relief are the observations of the nurses and the patient's family. Often, the patient will tell them much more than he will tell the doctor. The block may be repeated after two days have elapsed if there is no change in the pain pattern.

Since many of these patients have been receiving narcotics for varying periods of time and are addicted, this factor enters into the evaluation of the results of the block. Many patients will deny relief, even though it is present, in order to have an injection every four hours. Under no circumstances should they be abruptly cut off from narcotics, but the dosage should be gradually reduced to approach homeopathic levels or even none.

The duration of pain relief is variable. Some have complete relief for eight months or more, while some only for a few weeks. The usual duration of relief is three to four months. An occasional patient will have no change in his pain pattern at all after the block. When this occurs, it usually means the alcohol did not reach the posterior root in sufficient concentration to interrupt impulses. In this case, the procedure should be repeated. It is a rare patient who does not have some alteration of pain pattern under these circumstances.

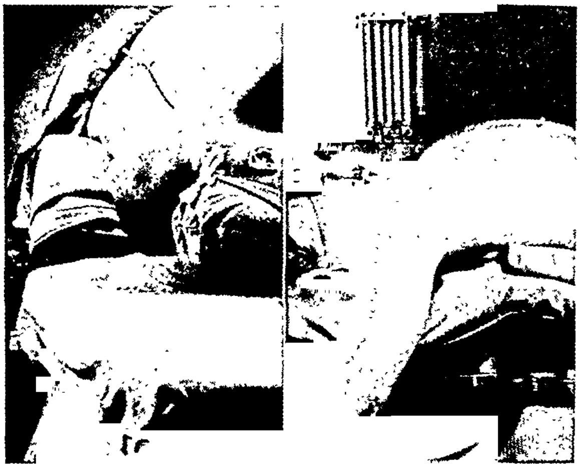

Fig. 3.—Position of patient for *(left)* block of left side and *(right)* bilateral block.

Complications are infrequent if the rate of injection, position of the patient, site of puncture, and technique are carefully observed. Headache and meningismus are rare and when they do occur are quite self-limited. The two most serious complications are those of muscle paralysis and bladder or rectal incontinence. The former is avoided if careful attention is paid to the position and rate of injection so that the alcohol is confined to the posterior root. Bladder incontinence, when it occurs, is usually transitory in nature and is handled easily with an indwelling catheter for a few days. Occasionally, there is marked proprioceptive sensory loss in the lower extremity which results in difficulty in walking. Again, this is a short-term loss and usually clears in seven to ten days.

Clinical Results

From June, 1956, to June, 1958, 106 patients received 174 subarachnoid alcohol blocks, with good results in 53 patients (50%), fair in 35 (33%), poor in 11 (10%), and no result in 7 (7%). Pain relief has been classified as good when complete relief is noted; fair, relief but with continued occasional narcotic demand secondary to addiction; poor, less pain but narcotics still needed; and no result, no pain relief at all.

In this group of 106 patients, there were only three complications of note. One was urinary incontinence, lasting four days, which necessitated the use of an indwelling Foley catheter. The other was a left deltoid muscle paralysis after a right subarachnoid alcohol block at the C-6 and C-7 interspace. This patient was known to have cerebral metastasis at the time, and death occurred two months after the procedure. The third was a paraplegia on the third day after a unilateral left block at the C-7 and T-1 interspace. This patient underwent a decompression laminectomy of T-1 to T-4 inclusive and was found to have a massive extradural metastatic carcinoma. At the time of the block, the needle apparently caused enough trauma in passing through this tumor to cause hemorrhage into it, which gradually compressed the cord at that level. This patient died three weeks after laminectomy, and at autopsy metastatic disease was found throughout the mediastinum and paraspinal area from C-5 to T-7. In four other patients, there was marked proprioceptive loss in the ipsilateral extremity. All of the latter cases resolved themselves without active treatment other than the patients' initiative in moving around.

Pathology

Ten spinal cords were obtained at autopsy. The time after alcohol block varied from three days to nine months. There were six females and four males, ranging from 8 years to the upper 70's, and each was in the terminal phase of malignant disease. In four instances four or more blocks had been done, while the remainder had a single procedure.

Demyelinization of the posterior roots, either unilateral or bilateral, was by far the most constant and outstanding finding. In three instances, degeneration of the axis cylinders was also encountered in the posterior root. Posterior root ganglions near the injected level showed moderate swelling and chromatolysis. The associated posterior roots showed severe demyelinization (fig. 4).

Within the cord itself, the most regularly affected areas were the fasciculus dorsolateralis (Lissauer's tract) and the posterior funiculus. The fasciculus dorsolateralis showed some degree of demyelinization in eight cases, while the posterior funiculus was involved in all but one. In many, the change was small and was represented by a narrow demyelinated band in the lateral part of the cuneate fasciculus at the level of the injection only. In others, there was much more extensive demyelinization occupying the entire thoracic column at the injection site and extending cephalad deviating medially in the cord. Below the site of injection, cells of Clarke's column were affected as were those of the posterior and lateral gray columns.

In brief, the above findings were consistent in all the cords studied. In eight additional cords, these findings were also noted. A more complete and detailed report will be published elsewhere on this aspect of subarachnoid alcohol block.

Comment

Constant pain extracts a terrific toll, both physically and emotionally, affecting not only the patient but those around him. The majority of patients in this study were physically incapable of withstanding another operative procedure or refused further operative intervention. In all cases, these patients had nothing to look forward to except a miserable, painful existence made somewhat easier by the liberal use of narcotics.

The most difficult aspect of any procedure for relief of pain is the assessment of the results therefrom. Patients with malignant disease not only are beset by physiopathological problems but also sustain a tremendous emotional upheaval as a result of the fact that they have a very serious disease which will probably be fatal to them. If these two facts are coupled with the overwhelming economic crises facing them in the course of their disease, it is not too difficult to see why they are unable clearly and rationally to evaluate discomfort relative to pain. These three factors, plus normal fluctuations in severity of pain, the difficulty of measuring pain accurately, and the inherent enthusiasm for the procedure in those attempting to alleviate pain make the degree of pain relief difficult to evaluate.

By its very nature, cancer is prone to spread by both a contiguous and distant manner. This means that pain may come from many areas at once with one locale giving more severe pain than others. Also, it means that one source of pain may be successfully blocked while a few weeks later another metastatic focus may be the source of pain at that time. With this in mind, it follows that any purely scientific criteria for evaluation of this type of pain relief are probably not suitable. When relief was obtained with narcotics, morphine, meperidine (Demerol) hydrochloride, and similar drugs were used. Many patients who experienced pain relief

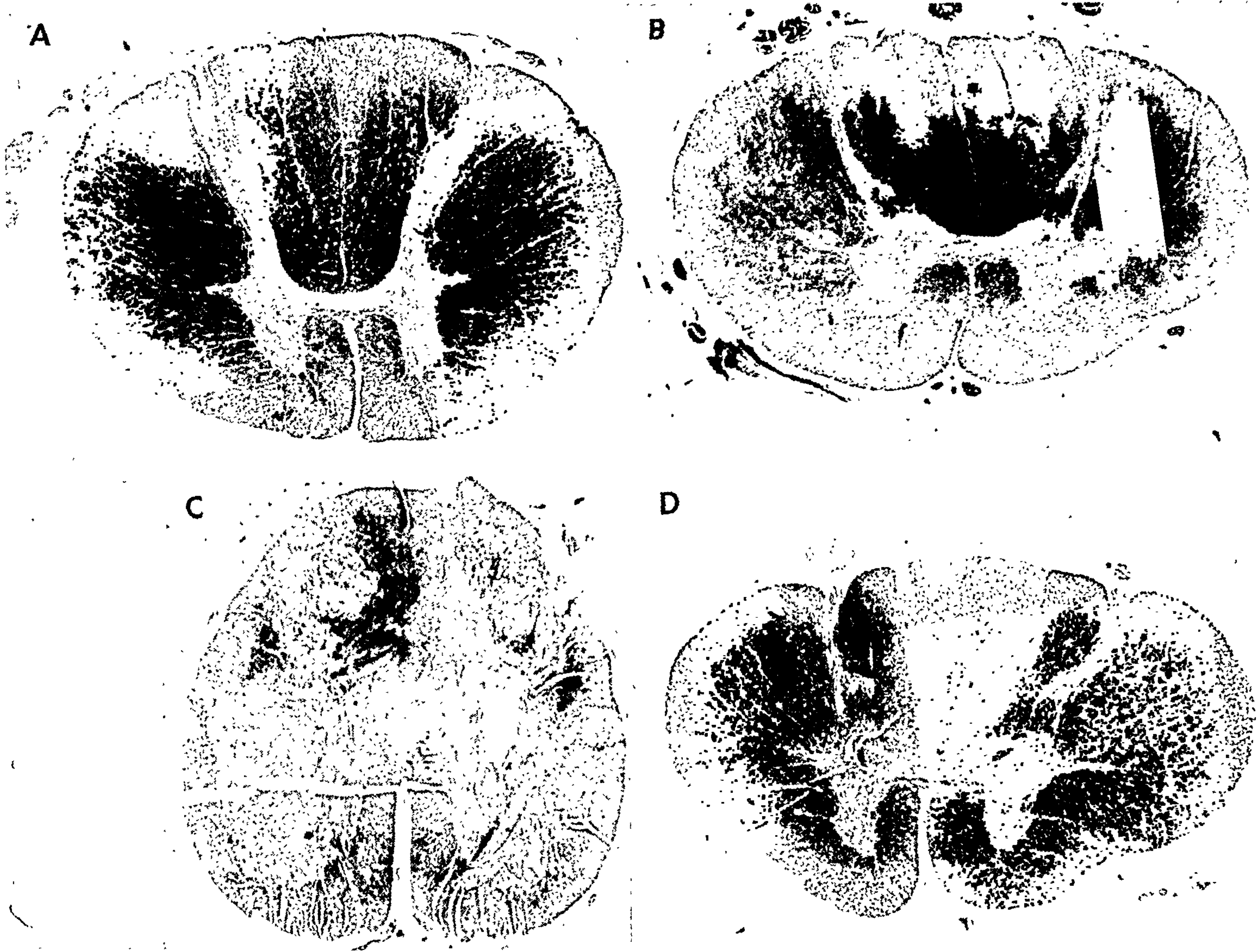

Fig. 4.—*A*, demyelinization of right dorsal root and adjacent wedge-shaped area of spinal cord at T-4. Such changes are considered to be result of direct contact of alcohol on cord. *B*, necrosis and demyelinization of dorsal part of posterior funiculus bilaterally (T-8). *C*, massive softening in left gray column and demyelinization in posterior and lateral white columns. It is believed that this resulted from accidental deposition of alcohol within cord. *D*, ascending degeneration in posterior funiculus at T-2. There was demyelinization of dorsal roots and lateral parts of posterior funiculus at T-3.

from the block needed analgesics, such as aspirin, a combination of acetophenetidin, aspirin, and caffeine (Empirin compound), and a preparation containing aspirin, aluminum glycinate, and magnesium carbonate (Bufferin), for complete comfort, while others who were receiving large doses of morphine or meperidine could receive dramatic reductions in dosage to one or two injections daily. The poor-result patients were those who had some alteration in pain pattern but who still needed a narcotic regularly, albeit in reduced amount, for comfort.

Summary

Subarachnoid alcohol block was performed in 106 patients with intractable pain due to malignant disease. There was a definite change in severity of pain in 83% of the patients, with 50% obtaining complete relief and 33% partial relief.

In 10 spinal cords examined at autopsy, the most constant finding was demyelinization of the posterior roots plus moderate swelling and chromatolyses of the posterior root ganglions. There were no complications of a lasting nature in any of the 106 patients in this series. Subarachnoid alcohol block is a worthwhile procedure in patients with intractable pain due to malignant disease. It is inexpensive; it can be performed by any skilled or well-trained anesthesiologist or neurosurgeon; and in such hands there will be few complications. It appears that subarachnoid alcohol block deserves a place in the physician's armamentarium in the constant war against the intractable pain of advanced malignant disease.

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H. Stephen Gallager, M.D., Department of Pathology, assisted in this study.

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MICROBIOLOGICAL TERMINOLOGY.—All nomenclatural codes agree that the scientific name of a species is made up to two parts. . . . The first component is a proper noun, in the singular number, which is the name of the genus in which the species is included. Botanists and bacteriologists agree that the second component is to be termed a specific epithet, but the zoologists have somewhat confused other biologists by their recent decision to call the second component the specific name. Why are other biologists confused? Because in bacteriology and botany the designations "species name" and "specific name" are synonymous. In zoology they are not, the specific epithet of the bacteriologist is the specific name of the zoologist. It should be clear that the specific epithet is not the name of a species, it is an explanatory word or phrase limiting the application of the generic name to a single species . . . [An epithet] . . . may be a single word which in some way defines or limits or modifies the meaning of the generic name or it may be a single phrase consisting of two or more words which together convey a single idea, but which do not separately modify the generic name. The codes of nomenclature specify clearly that a specific epithet may be one of three types: 1. An adjective (simple or compound) which directly modifies the generic name, and agrees with it in gender, number, and case. As Sarcina lutea, the yellow Sarcina. 2. A noun in the genitive modifying the generic name. It need not agree with the generic name in gender or number. As Escherichia coli, the Escherichia of the colon. 3. A noun in apposition with the generic name. It agrees in case with the generic name, but need not agree in gender. As Xanthomonas prunicola, Xanthomonas the plum dweller.—R. E. Buchanan, Microbiological Literacy, *Bacteriological Reviews*, September, 1958.

CLINICAL NOTES

STOMATITIS AND PROCTITIS AS MANIFESTATIONS OF MEPROBAMATE IDIOSYNCRASY

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The incidence of serious untoward reactions to meprobamate must be small in view of the widespread use of this drug. The following case is reported because it is believed to represent the first recorded instance of such a reaction to meprobamate. Furthermore, it represents a rare type of reaction to any drug.

Report of a Case

A 51-year-old woman was admitted on June 23, 1958, to *Woman's Hospital, Philadelphia, because of a myocardial* infarction. She was treated in the conventional manner with bed rest and bishydroxycoumarin (Dicumarol); in addition, her previous medication with chlorothiazide, 0.5 Gm. daily, and digoxin, 0.5 mg. daily, was continued. Pentobarbital was given nightly, but, starting on July 8, chloral hydrate was substituted. Because of continued restlessness during the day, as well as sleeplessness, therapy with meprobamate, 400 mg. given four times a day, and secobarbital and phenobarbital given at bedtime was started on July 11. The patient received two tablets of meprobamate on that day, and the next morning she remarked vaguely to a house officer that she was "allergic to tranquilizers" and that her mouth felt sore. Meprobamate therapy was therefore discontinued, but that with the other drugs was maintained. A few shallow ulcers were noted on her oral mucosa on July 11. By July 14, this had progressed to extensive sloughing ulceration of the mucosa of inner cheeks, tongue, and palate. The patient complained of severe soreness of her mouth, to the point that she had difficulty swallowing liquids, as well as general malaise and severe itching and burning of the anal area. Her temperature rose to 100.4 F (38 C); she appeared acutely ill. Her cervical lymph nodes were swollen and tender. The dental consultant felt that the lesion was typical of necrotizing ulcerative (Vincent's) stomatitis but that acute moniliasis and herpetic stomatitis should be ruled out.

On July 15, she noted one episode of frank anal bleeding ("about 2 teaspoons" of bright blood). She had no other gastrointestinal signs or symptoms. Because of her cardiac status, it was thought wise to postpone sigmoidoscopy and barium studies.

At this point additional history revealed the nature of the patient's previous meprobamate reactions. In July, 1957, she had been given meprobamate for the first time. She took a total of 400 mg. of meprobamate, and within 24 hours she had extensive blistering of mucosa of the lips and tongue, as well as severe itching and burning in the oral area. She was assured then that this was unrelated to the drug. Apparently syphilis was suspected, but darkfield examination and serologic testing gave negative results. In March, 1958, after ingestion of a single tablet of meprobamate, her mouth "felt severely swollen" but this gradually subsided. An extensive history failed to disclose stomatitis on any previous occasion, intolerance to other drugs (including barbiturates) or foods, or any typical allergic symptomatology.

In view of this history, cortisone acetate medication was started, 50 mg. by mouth every four hours. This was done with some trepidation lest an infectious process be aggravated by this therapy. However, the patient improved markedly in 24 hours; her fever and adenopathy subsided. The extensive ulcerations gradually improved in the ensuing days, during which time cortisone dosage was slowly tapered off and then discontinued. Therapy with the barbiturates and the cardiac drugs was continued during this whole period. Microscopic and darkfield examination of a mouth swab on July 14 were later reported as negative for fungi and Vincent's organism, and only streptococci and staphylococci could be cultured from it.

Comment

The problem of meprobamate idiosyncrasy has been thoroughly reviewed recently by Charkes.[1] He points out that about 1 patient in 200 may respond to an initial administration on meprobamate with an anaphylactoid response. In a series of 113 cases of meprobamate idiosyncrasy that he collected from the literature, a cutaneous reaction appeared as early as 15 minutes or as late as one week after the initial dose. The rash was erythematous, maculopapular or urticarial, or a combination of these. Systemic symptoms were also present in a number of cases. Of eight reported skin tests (patch or scratch), six showed completely negative findings. A patch test also showed negative findings in our case. An oral mucosal test may be more informative, but it requires some experience for performance and interpretation.[2] A "latency" period, arbitrarily set at two weeks after the first dose, may serve to separate cases of true allergy from mere idiosyncrasy.[1] Antihistaminics have not resulted in dramatic relief in these conditions. Steroid therapy often has been helpful. In our case, steroid medication produced marked relief from both the generalized "toxicity" and local reaction. Levan [3] states that the cutaneous reactions of meprobamate are characterized by (1) their early appearance (sometimes as early as 15 minutes); (2) a severe erythematous rash, at times purpuric, tending to be particularly severe in the groin; and (3) associated marked weakness, faintness, and transient but recurrent syncope.

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To our knowledge, no case of meprobamate idiosyncrasy with mucocutaneous manifestations consisting solely of stomatitis and/or proctitis has been reported. This reaction must be extremely rare in view of the tremendous use of this drug. Two major manufacturers had no knowledge of such type of reaction.[4] In view of this rarity, local and other etiological factors should be carefully considered before a case of stomatitis or proctitis is attributed to the coincidental intake of meprobamate. On the other hand, Charkes[1] emphasizes that with the administration of a test dose the second reaction could be much more severe than the first. This was inadvertently demonstrated in our case. If it is imperative to give such a test dose, no more than a small amount (50 mg.) should be tried.

Summary

A case of stomatitis and proctitis developed on several occasions after administration of meprobamate. In the last instance the reaction was severe, progressed in spite of withdrawal of the drug, and responded to cortisone therapy.

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BUCCAL AND SUBLINGUAL ADMINISTRATION OF HEPARIN POTASSIUM (CLARIN)

STUDIES OF PLASMA TRIGLYCERIDE LIPOLYSIS AND HEPARIN LEVELS

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The discovery of the clearing of alimentary lipemia after the injection of heparin[1] and the demonstration of long-term efficacy of intermittent, parental administration of heparin in reducing the anticipated mortality of elderly patients with severe coronary atherosclerotic disease[2] aroused interest in the possible role of this physiological substance in fat transport and in its use as prophylactic therapy in hyperlipemic and hypercholesterolemic states. If heparin were effective by mouth, it would probably be the drug of choice in all patients with clinically diagnosed atherosclerosis. Therefore, the original report[3] of the absorption of sublingually given heparin attracted widespread attention. Unfortunately, these findings were not confirmed.[4] Subsequently, Italian authors reported a 20% absorption of buccally given heparin with an effect on lipoproteins but not on coagulation.[5] Recently, clarification of postprandial lipemia after the use of heparin potassium tablets was demonstrated as an exhibit,[6] and the product used (Clarin Linguets) has been subsequently released on the market.

The use of serum optical density levels as an index of the rate of removal of fats from the blood stream after standard fat meals affords suggestive but not conclusive results, since variations in intestinal absorption may affect the findings, and optical density may decrease without a concomitant reduction of the lipid content of the plasma. Moreover, when medicaments are given which may contain mucinous substances, the measurement of lipemia by optical techniques is entirely inadequate, since mucins may clear lipemic plasma through physical effects without fat lipolysis or fat removal taking place.[7] Accordingly, the experiments reported in this communication were designed to avoid these pitfalls by evaluating triglyceride lipolytic activity in vitro and by measuring plasma heparin potassium content directly before and after use of the drug.

Method of Study

Twenty-one subjects were studied. Blood was drawn in the fasting state and 45-60 minutes after the buccal or sublingual administration of the heparin potassium tablet, containing 1,500 units of heparin potassium (when it was almost all dissolved). In several instances a third blood sample was taken one hour later. Fasting blood was used since it has been shown that after heparin is given the lipemia clearing factor (lipoprotein lipase) is inactivated during the fat-splitting process.[8] Therefore, if neutral fat had been available as substrate in the blood, and in vivo lipolysis consequently occurred, small amounts of enzyme activity after administration of heparin could be missed by in

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vitro techniques. In nine subjects, a small dose of heparin was given intravenously after the second blood sample was taken and blood was again withdrawn in 10 minutes. Oxalated plasma was separated in a refrigerated centrifuge and lipemia clearing and lipolytic activity immediately determined with use of coconut oil and ultracentrifugally separated human low-density lipoproteins as fat substrates, according to previously described techniques.[9] In 13 subjects the plasma heparin potassium content was extracted and measured [10] before and after heparin potassium administration. The Lee-White method of determining clotting time was used on all blood samples.

Results

The results of the plasma lipemia clearing and lipolytic activity studies are shown in table 1. It is apparent that triglyceride splitting with release of fatty acids may occur without any evidence of clearing of coconut oil substrates. Therefore, the most sensitive and significant findings are shown in the last column of the table. In five subjects (cases 1, 2, 3, 7, and 13) there was evidence of more lipoprotein lipase activity after the heparin potassium administration than before, although in only three of the five was it of substantial proportions. In all seven subjects given 2-16 mg. of heparin potassium intravenously and in one of two given 1 mg. intravenously, increased clearing and lipolytic activity occurred. The next to the last column is included since it was possible that lipolysis occurred in the test tube as soon as lipoproteins were added and that it therefore might not be found during the one-hour incubation period. Thus, the substantially increased control fatty acids after the drug was given in the patients in cases 4, 10, 11, and 15 may indicate the presence of postadministration enzyme, although this is not certain. In summary, there was definite evidence of heparin potassium absorption and consequent substantial fat-splitting activity in three subjects and possible trace activity in six others after use of the tablets. It is of interest to point out that the patient in case 16 shows a clear example of nonlipolytic clearing and that the increased clearing without increased fat-splitting seen in the patients in cases 12 and 19 after the drug was given may represent the same phenomenon.

Table 2 presents the results of the heparin potassium assays in 13 subjects. The method has a ± 15% deviation from the mean. Thus, there is definite evidence of heparin absorption only in the patient in case 7. In contrast, the marked increase in the patient in case 21 after 2 mg. of heparin potassium was given intravenously is obvious. It is apparent that the method is not sufficiently discriminating to measure the small amount of heparin that must have been absorbed in the patients in cases 1 and 3, although the increase was shown in that in case 7. Nevertheless, since 2 mg. (200 units) given intravenously resulted in a 50% elevation (5.5 units %) in the circulating heparin potassium level, it would appear that less than 100 units (of the 1,500 units in the tablet) was present in the blood at the height of tablet's dissolution even in patients who showed lipolytic activity.

TABLE 1.—*Fasting Plasma Optical Density, Lipemia Clearing and Lipolytic Activity, and Free Fatty Acid Before Incubation, Before and After Sublingual and Intravenous Administration of Heparin Potassium*

Case No.	Age, Yr.	Sex	Fasting Blood Sample	Plasma Optical Density	Lipemia Clearing Activity, Maximum Rate of Clearing per Hr.*	Control Free Fatty Acids (Plasma plus Added Lipoproteins)	Plasma Lipolytic Activity, Maximum Rate of Free Fatty Acid Release, mEq./Liter/Hr.†
1	80	F	Control	0.03	0	1.9	0.3
			After tablet	0.03	0	2.0	2.0
2	45	M	Control	0.08	0	1.2	1.0
			After tablet	0.03	0	1.2	1.4
3	57	F	Control	0.03	0	2.2	0
			After tablet.	0.03	0	2.3	1.2
4	50	M	Control	0.03	0	2.0	0
			After tablet	0.03	0	2.3	0
5	55	M	Control	0.04	0	1.1	0.2
			After tablet	0.04	0	1.1	0.2
6	64	M	Control	0.06	3	1.1	0.8
			After tablet	0.04	1	1.1	0.8
7	60	F	Control	0.03	0	2.0	0
			After tablet	0.03	0	1.6	1.0
8	62	M	Control	0.03	0	1.7	0
			After tablet	0.03	0	1.7	0
9	59	M	Control	0.04	0	1.4	0
			After tablet	0.01	0	1.4	0
10	34	F	Control	0.02	18	1.6	0.4
			After tablet	0.03	12	2.1	0.4
11	55	F	Control	0.07	0	2.5	0
			After tablet	0.08	0	3.1	0
12	24	F	Control	0.04	2	1.4	0.4
			After tablet	0.04	4	1.4	0.4
13	61	M	Control	0.06	0	1.4	0.1
			After tablet	0.05	0	1.4	0.4
			After 13 mg. I.V.	0.05	42	2.2	9.2
14	49	M	Control	0.06	6	1.6	0
			After tablet	0.05	6	1.6	0
			After 13 mg. I.V.	0.04	54	3.1	6.0
15	49	M	Control	0.03	0	1.1	0.4
			After tablet	0.03	0	2.0	0.4
			After 16 mg. I.V.	0.03	60	...	...
16	68	F	Control	0.04	18	0.9	0
			After tablet	0.04	18	0.9	0
			After 2 mg. I.V.	0.03	18	1.6	0.4
17	32	F	Control	0.03	0	1.3	0
			After tablet	0.03	0	1.5	0
			After 2 mg. I V.	0.03	12	...	...
18	47	F	Control	0.05	0	1.3	0
			After tablet	0.04	0	1.3	0
			After 2 mg. I.V.	0.04	12	2.2	1.2
19	20	M	Control	0.04	3	1.0	0
			After tablet	0.04	6	1.0	0
			After 1 mg. I.V.	0.03	15	1.0	0.2
20	21	M	Control	0.04	18	1.1	0
			After tablet	0.04	18	1.1	0
			After 1 mg. I.V.	0.03	18	1.1	0
21	32	F	Control	0.02	6	1.5	0
			After tablet	0.02	6	1.4	0
			After 2 mg. I.V.	0.02	36	1.9	1.4

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*Measured in Coleman Jr. spectrophotometer at 700 mμ every 10 minutes for one hour at 25 C.; 1 ml. of plasma + 0.1 ml. of 1% coconut oil (Ediol).

†5 ml. of plasma + 1.0 of ml. human low-density lipoproteins incubated at 37 C for one hour; aliquots analyzed every 15 minutes.

The results of the clotting time determinations are not shown, as no definite anticoagulant activity was found after administration of the heparin potassium tablets.

Comment

In view of the difference between the findings in the present study and those previously presented,[6] it is worthwhile to discuss possible criticisms of these experiments and the in vitro technique used. It may be argued that the effect of sublingually given heparin is delayed in some manner. However, it is reasonable to believe that absorption would be maximal when the tablet was fully dissolved. Furthermore, although the results were not shown in the table, in several instances a third blood sample was also taken one hour after the tablet had melted. The results were no different than in the first post-tablet test. Furthermore, it is possible that ultracentrifugally separated low-density lipoproteins are not as easily acted on by the postadministration factor as natural in vivo chylomicrons. However, the same lipoproteins were rapidly split by blood plasma drawn after 2 mg. of heparin was injected intravenously, thus proving their adequacy as a fat substrate. It thus is more likely that the discrepancy in the results is due either to the nonlipolytic fat-clearing action of other mucinous polysaccharides[11] or to the failure of the original investigator of heparin potassium[6] to use placebo tablets in his control observations. The tablets were composed of crude heparin, not highly refined, and probably contained mucins similar to heparin in basic structure. The failure of larger doses of sublingually given heparin to enhance the lipemia-clearing effect[12] or to result in any anticoagulant activity is further evidence against any substantial absorption by this route. It has been shown that, except for minimal doses below 3 mg., there is no support for the view that the amount of heparin required to influence the clotting mechanism is greater than that required for lipemia clearing.[13]

Table 2.—*Fasting Plasma Heparin Potassium Levels Before and After Administration of Tablets*

Case No.	Heparin, Units %*	
	Control	After Tablet
1	12.5	12.0
2	16.0	15.0
3	14.5	14.0
4	12.0	12.5
5	13.0	11.5
6	14.5	13.0
7	10.0	12.5
8	12.0	12.5
9	12.5	13.5
10	12.0	12.5
12	12.0	12.5
13	15.0	14.0
21†	11.0	11.5

*Average of duplicate determination.

†Level was 17 units % after intravenous administration of 2 mg. of heparin potassium.

Heparin potassium, in the present study, was absorbed in doses large enough to produce substantial amounts of fat-splitting enzyme in only 3 of 21 patients—possibly trace amounts in another 6 subjects. In 12 of the 21 there was no evidence that heparin potassium had penetrated the mucosal barrier. Thus, from the practical standpoint, this route of heparin administration is uncertain and inadequate. Even if 20% of buccally given heparin were absorbed, as has been stated,[5] this mode of administration would be extremely wasteful. Furthermore, it is a long step from the clinically demonstrated beneficial effects of large doses of injected heparin in severe atherosclerotic disease[2] to the unproved virtues of minimal lipemia clearing.

Summary

The effect of heparin potassium tablets (Clarin Linguets) has been evaluated in 21 subjects by in vitro measurements of lipolytic activity and by determination of plasma heparin potassium levels. In 3 subjects there was moderate absorption of the heparin potassium, in 6 possibly trace absorption, and in 12 no evidence of absorption of buccally given heparin potassium. These results indicate that orally given heparin potassium tablets are ineffective in 85% (18 of 21) of patients and that parenterally given heparin should be used when this type of therapy is indicated in patients with atherosclerotic disease.

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ASPIRATION OF AMNIOTIC FLUID OF THE PERINATE

NEW CONCEPT OF AN OLD DISEASE

Robert P. Barnett, M.D., Spokane, Wash.

Obstetrics has advanced to the point where the maternal mortality is less than 1%. It is both amazing and shameful to find an unchanged perinatal morbidity and mortality during the first 7 days of life in the last four decades.

Most of the literature on atelectasis and hyaline membrane disease in the perinatal period is concerned with the secondary chemical causation. Just as much is concerned with treatment of lung pathology, cardiac failure, elevated pCO_2 levels, anoxemia, and cerebral anoxia of an elective section of the premature infant and the infant of a diabetic mother.[1] Very little information has been offered concerning primary mechanical etiology and its immediate treatment.

At the risk of being practical, I believe the realist has the proper answer. How can one hope to bypass with oxygen the alveoli and/or bronchi and bronchioles two hours or later after birth? Treatment should be directed to the immediate care of the perinate (infant at birth)—not two or more hours later. By that time the amniotic fluid is well fixed in the alveolar walls and the bronchial tree.

In the full-term baby delivered by section, when the mother has had no labor, it is possible to aspirate from the stomach and tracheobronchial tree from 30 to 60 cc. of amniotic fluid with a soft rubber catheter. It is interesting to note that, from the average full-term infant delivered per vaginum, approximately 5 to 15 cc. of amniotic fluid can be obtained in the same way.

Therefore, the first recommendation to reduce morbidity and mortality in the perinate would be routine aspiration of the stomach contents with intermittent compression of the abdomen. A soft rubber catheter introduced two or three times will suffice. Tracheobronchial aspiration should not be considered routine but should be left in the hands of those who are experienced.

A simple method used by many physicians is recommended and can be described as follows: While awaiting placental expulsion and after gastric aspiration, the physician can introduce an infant laryngoscope into the oropharynx and gently lift the epiglottis. Then, with exposure of the trachea, the soft rubber catheter can be placed in the hypopharynx and a nurse can apply gentle artificial respiration on the anterior chest wall while the physician aspirates the amniotic fluid as it presents itself in the hypopharynx and the trachea. This is especially applicable to the premature infant because of injury to the trachea, even with a soft rubber catheter, and the time consumed by tracheobronchial aspiration in these weak infants.

The second recommendation, and I believe an imperative one, is that the infant, during the perinatal period (15 days), should be in the supine position only when the diapers are changed and in a few other exceptional cases—all should be done under close observation. This is particularly true during the first 3 days of life. In the nursery for newborn infants, thousands of times physicians and nurses have "just accidentally" seen an infant cyanotic and gasping while lying in the supine position. It should be mandatory that all infants be changed from side to side and to prone positions frequently. This also applies to the premature infants who appear to tolerate the prone position.

In a moribund perinate the head up or head down position in the nursery can be considered dangerous. There is great risk of the head falling

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From the Pediatric Service, St. Luke's Hospital.

on the anterior chest wall and occluding the airway. However, in the healthy full-term baby, head up or head down positions should be left to the discretion of the individual physician.

Elective section mortality remains at 5 to 10% over the United States and has not been altered in the past 10 years. The incidence of cerebral palsy due to anoxemia and cerebral anoxia remains unchanged.

We will find that the primary mechanical etiology of aspiration of amniotic fluid in the newborn infant should receive prompt attention and treatment, instead of treatment of the secondary complications. This late treatment will only serve to continue the present situation.

With these simple delivery room and nursery techniques, carried out as a routine, we can reduce the infant morbidity and/or mortality by 50% in any of our general hospitals.

512 Medical Center Bldg.

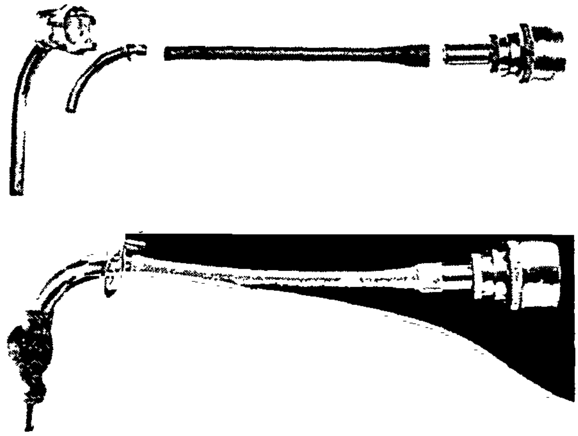
Reference

1. Fifth M & R Pediatric Research Conference, St. Christophers Hospital For Children, Philadelphia, April, 1952.

RESPIRATOR TRACHEOTOMY TUBE

William J. Loeb, M.D., Cleveland

Any general hospital treats patients who require respiratory assistance for reasons ranging from intracranial disease or injury with central respiratory depression, excessive drug intake, thoracic injury, or pulmonary insufficiency to unidentifiable causes. The problem involved is not one of mechanical airway improvement alone but also one of insufficient central respiratory stimulus. In coping with this problem a modified tracheotomy tube has been in use which in my experience has provided added control of respiratory exchange to tide the patient over a critical period until he can resume adequate respiration without assistance.



Top, component parts of tracheotomy tube. *Bottom*, assembled tube and fittings.

The use of a respirator with the familiar naso-oral mask is difficult because it precludes airway aspiration. Tracheotomy alone may not be enough because artificial respiratory control cannot be well maintained unless a closed system is provided. The tube which we have used (see fig.) consists of a cane-shaped tracheotomy tube made ⅜ in. (0.96 cm.) shorter than standard. The inner cannula is provided with a ⅜ in. extension beyond the base plate. To this a fairly stiff rubber tube is connected, at the other end of which a standard slip fitting is provided. This may be connected with a respirator. An inflatable rubber cuff (see figure) as is used in anesthesia is placed around the outer cannula. Inflation of this provides an airway which is completely under respirator control, avoiding leaks.

The flexibility of the tube placed between the inner cannula and the slip fitting permits some motion by the patient without disconnecting the slip joint from the respirator. Hitherto it has been difficult to use the respirator connected directly to the tracheotomy tube but this inner cannula and flexible tube may be quickly removed for tracheal suction and replaced without loss of significant respiratory exchange.

These tubes, in sizes 1 through 7, have been used successfully at Mt. Sinai Hospital. There has been minimal irritation of the trachea, even in patients who are conscious.

10300 Carnegie Ave. (6).

From the Department of Oxygen and Inhalation Therapy, Mt. Sinai Hospital.

View of a session at last month's Annual Congress on Medical Education and Licensure, attended in Chicago by more than 1,000 physicians and other interested registrants. In scene above, Dr. William H. Hubbard Jr. of New York University College of Medicine discusses "The Role of Research in the Education of All Physicians."

MEDICINE AT WORK

- *Research and Specialism*
- *Doctor to Doctor Via FM*
- *Working with Engineers*
- *New Kind of Homemaker*
- *Relative Value Studies*
- *Lawyers Discuss Doctors*

Careers in Health

Are there any budding orthoptic technicians among the students in your local high school? Probably not—a career as an orthoptic technician is so new that few have heard of it. This is one of the reasons that recently led the Connecticut State Medical Society to inaugurate "Connecticut Health Careers."

Aided by its Woman's Auxiliary and other health organizations, the society's program is designed to acquaint high school students with career opportunities growing out of advances in medical research, hospital practice, and patient care.

The nucleus of the program was the Auxiliary's past efforts in advancing nursing as a career. When the current project was begun last fall on an experimental basis in a few schools, it showed such promise that it is now being activated on a statewide basis. It covers as many as 50 career occupations. Speakers, films, field trips to hospitals and laboratories, and a variety of publications are ingredients of the program.

Cooperating groups include the Connecticut Hospital Association, the Connecticut League for Nursing, the Connecticut Society of Pathologists, the American Registry of Technicians, the Connecticut Public Health Association, and the A. M. A.

Dr. Harry C. Knight, chairman of the Society's committee to develop the project, is enthusiastic about early results. He said: "We have found a welcome interest, and the future looks bright."

'To Find Fault with Ourselves'

Stethoscope on Specialism and Research in Medical Education

> We are gathered here today to find fault with ourselves in order to strengthen our education by correcting our weaknesses. . . .
>
> Modern specialization, fostering security in a tight little compartment, has reduced the scientist to a role without individuality. . . .
>
> The practicing physician has a magnificent opportunity and duty to observe patients and add to the fundamentals of our knowledge of disease. This is also truly "research." . . .
>
> Some students may see in medicine a highly lucrative career and yearn only for the diploma as a certificate of a gilt-edged credit rating. These are not likely to be really educated by any method and it is best that they be denied admission to medical training. . . .

Those statements are a sampling of the combined provocativeness-introspection-experience-learnedness atmosphere which surrounded 1,048 participants at last month's 55th Annual Congress on Medical Education and Licensure. No holds were barred as several score speakers and workshop conferees prominent in and related to medicine and education sailed into broad phases and intense impacts of specialism and research. The place and perspective of research and specialism in the education and practice of medicine formed the motif of this year's Congress.

The Congress, Feb. 7-10 in Chicago, was sponsored by the A. M. A. Council on Medical Education and Hospitals in cooperation with the Association of American Medical Colleges, the Federation of State Medical Boards of the United States, and the Advisory Board for Medical Specialties. A highlight of the meeting was a three-point stimulus, suggested by A. M. A. President Gunnar Gundersen, "to insure" that all practicing physicians regularly keep abreast of important developments in medicine. He recommended that:

—Medical license holders be required to regularly participate in acceptable postgraduate programs.

—Holders of medical licenses be required at intervals to demonstrate, through reexamination, their retention of important basic knowledge and competencies, and their awareness of significant advances in medicine.

—Reexamination and/or postgraduate education be required "for continuing membership in organized medicine, specialty and other medical organizations."

"I am not at all certain which of these methods is best," said Dr. Gundersen. "The first [reexamination] would produce the quickest results, but there is no assurance it is best. This is a matter for careful study . . . not in 1965 or 1975 or some later date. The public and profession must be assured now of the high standards and qualifications of physicians." Dr. Gundersen also brought out these points:

Medical men must work cooperatively with others or have others superimpose a way of medical life that may give medicine little voice.

There is a need for the extension of a uniform policy of endorsement or reciprocity of medical licenses.

Medical educators and others should explore the feasibility and desirability of requiring at least two years of approved hospital training after medical school ("one year is not adequate preparation") before being eligible for full licensure.

Following are excerpts from other presentations:

EDUCATION'S SCOPE AND SPAN—

The introduction of the longer hospital period of training plus the requirements of military service after graduation have intensified the challenge to reduce the long span of professional education. The most satisfactory solution may be not to interfere with the medical course per se, which is currently undergoing intensive revisions and improvements, but to strengthen and vitalize the period of secondary and college education.

—Willard C. Rappleye, M.D., President,
Josiah Macy Jr. Foundation

For a long time the vacuum represented by the high school will remain a heavy drag on medical education. For all practical purposes the three to four years in college only enable medical students to obtain knowledge which should have been obtained in a high school of good standing. . . . The medical student of today should be educated not only for the year 1959 but also for the four following decades, because he will probably still practice medicine in the year 2000. The knowledge of today will be ridiculous in 40 years.

—Isidore Snapper, M.D., Beth-El
Hospital, Brooklyn, N. Y.

If you are five years behind in your thinking now, you are more out of date than your fathers would have been if they were 25 to 50 years behind in their thinking. You have to run faster and faster to stand still. . . . We can stockpile medical supplies and equipment. We cannot stockpile doctors. That is why strong programs of medical education are so vitally necessary.

—John S. Patterson, Deputy Director,
Office of Civil and Defense Mobilization

LIMITS AND EXPANSE OF SPECIALISM—

One of the lasting tributes to the genius of the great classic figures in medical science is the ingenuity they displayed for inventing not only new techniques but often whole new concepts in fields quite outside their own. But the climate has changed. The solution (of a problem at hand) would seem now to be as simple as adding one more "specialist" and congratulating oneself that the approach is

This Matter of Resident Pay . . .

There were four workshop conferences in conjunction with the Annual Congress on Medical Education and Licensure last month and not one was scheduled to look into the economic problems of residents. Yet, these very problems popped up at three of the sessions, and were duly noted.

One summary report stated: "It was agreed that residents are underpaid and that some had to work out of hours for pay to support wife and family." Another noted: "There is no doubt that many who wish to continue residency training are unable to do so because of financial handicaps and are unable to borrow." And, according to a third workshop summation: "Young men and women in residencies should be looked upon as graduate students and their economic needs should be met from that point of view rather than from the point of view of their contributions to hospital service."

Discussions were not all in that vein, however. A participant on one panel, Columbia University Sociologist Patricia Kendall, told of her findings on medical student attitudes: "The quality of teaching was by far the most important consideration that led them to choose a particular hospital for their internship and residency. Salary ranked very low in their stated considerations."

Another workshop group agreed that whatever the source or amount of resident pay "it is perhaps forgotten that in one way or another the cost is ultimately passed on to the patient." When the question was raised whether high compensation would help or hurt, the conferees said they detected some feeling that "too high levels of payment might lead to undue prolongation of periods of resident training." A physician on that panel said, "In my day, as residents, we felt we were lucky to get what we got. Our babies were our own responsibility and not the community's. Residents should have enough to live but demands need not be met in toto."

Two other physicians felt that the problem was indeed serious but not being portrayed in proper perspective. They reported: "Although salary is not usually the major inducement for choosing a particular residency, lack of adequate funds often requires the resident to make compromises in his career plans. And these compromises frequently limit his potential development."

One of four workshop conferences in session during Annual Congress. This one discussed "The Specialty Board."

"modern" because it shows evidence of "multidisciplinary integration."

—S. Marsh Tenney, M.D., Dartmouth Medical School

Only by concentrated, competent, and enlightened attack at numerous limited areas as they open up to us as we continue investigation can we ever hope to begin to understand the whole. By this token one can confidently predict that true specialism in science will continue to survive and multiply.

—Paul M. Gross, Ph.D., Vice-President, Duke University

Specialism is in effect threatened by its own technological instrumentation. I cannot envision automation taking over the surgeon's work, but it may well take over that of the anesthetist.

—Iago Galdston, M.D., New York Academy of Medicine

Only when specialization is premature, or is disassociated out of context with the whole, does it have an adverse effect. This is as true of the mechanic who tightens one bolt on an assembly line as it is of the doctor who gazes into only one orifice of the body.

—Herman Pearse, M.D., University of Rochester School of Medicine and Dentistry

Now and again the medical profession will single out a general practitioner toward the close of an honorable career and give him public honors, but there is something sentimental and nostalgic about this gesture. It is as though there had been introduced the practice of honoring the knight of the year during the late middle ages after the invention of gunpowder and firearms. . . . The important consideration is the way in which the specialty is taught. All too often the approach is too restricted. It is too often directed toward producing the clever technician and not the educated expert. What I suggest is that the proper human use of a specialty should be approached as a function not simply of the physician as a good man but of the specialist as a good physician.

—Moody E. Prior, Ph.D., Dean, Northwestern University Graduate School

RESEARCH—MOTIVE AND PRACTICE—

Every student has his own set of motivations. Some may see in medicine a highly lucrative career. Some may be highly motivated by a desire for service. A third group might include those who marvel at the wonder of nature that is man and want, more than anything, to understand more and more about this creature—it undoubtedly will be one of them who will help unravel the mystery of cancer, help us stem the deterioration of aging, help reverse the trend in mental illness. Their satisfaction is not in direct service but in indirect service.

—Conrad A. Elvehjem, Ph.D., President, University of Wisconsin

Research has been described in many ways. I like a recent definition of Bernard Greenberg's, "a burning yearning for learning." If the first letter of the last word is omitted, one sees clearly the common motive for violation of the essence of research. Too often research studies become the legal tender of academic life.

—Nathan A. Womack, M.D., University of North Carolina School of Medicine

SOCIOECONOMICS—

Medical insurance has had a catastrophic effect on residency training in surgery. In most university-owned teaching hospitals and in most private hospitals, insurance has converted the clinic into private patients. . . . The straightforward approach is to have the residents licensed to practice, and approved for the care of insurance patients. If a fee is involved it is accredited to the surgical staff, who should act as trustees of such funds. Unless something is done the public will become the unsuspecting subjects of inadequately trained surgeons. We must find a way to retain the benefits both of medical insurance and of the residency system of training.

—Herman Pearse, M.D.

Although many of our future interns have only modest means and are at the same time burdened by financial obligations, they clearly prefer the hospitals which offer a poorly paid internship with a well-integrated teaching program, and shun the hospitals where there are higher emoluments but where they will be abused as scribblers of medical charts.

—Isidore Snapper, M.D.

The changing social character of the student is probably responsible in part for the change in the attractiveness which medicine holds for him. If we fail to attract into medicine an adequate number of topnotch students who can acquire and use the broader and deeper understanding of basic biology and behavioral sciences in the care of patients, our educational program will of necessity have to lower its goals to fit the students with which it is provided.

—John A. D. Cooper, M.D., Northwestern University Medical School

Selected full texts of presentations at the Congress will be published in future issues of THE JOURNAL.

The Council on Medical Education and Hospitals is headed by Dr. Leland S. McKittrick of Brookline, Mass. Other members are Drs. W. Clarke Wescoe of Kansas City, Kan.; John Z. Bowers of Madison, Wis.; James M. Faulkner of Cambridge, Mass.; Warde B. Allan of Baltimore; John W. Cline of San Francisco; Harlan English of Danville, Ill.; Charles T. Stone Sr. of Galveston, Texas; Guy A. Caldwell of New Orleans; and W. Andrew Bunten of Cheyenne, Wyo. The Council Secretary in Chicago is Dr. Walter S. Wiggins.

Education Via FM Radio

Neither Weather Nor Work Keeps These Doctors from Their Studies

Richard P. Pratt

The temperature hovered in the mid-twenties and there was snow on the ground when nearly 100 physicians of New York's Hudson River Valley met at noon to hear a postgraduate medical conference on the treatment of acute vascular catastrophes.

Drs. Samuel Powers, professor of experimental surgery, and G. Rhemi Denton. assistant professor of surgery, spoke for 20 minutes and answered questions in an informal atmosphere. A mild note of humor was injected when one participant asked Dr. Powers to identify the ingredients of a "cocktail" sometimes given intravenously in cases of pulmonary infarct.

The session might have been indistinguishable from hundreds of other postgraduate offerings had it not been for one factor: the hour-long program was conducted entirely via a two-way FM (frequency modulation) radio system operated by the Albany Medical College. The faculty spoke not from behind a lectern, but in front of a microphone. Members of the audience were not forced to travel great distances to attend; participants listened—and asked their questions—from comfortable meeting rooms in eight New York hospitals, and some even managed to eat lunch during the period. All were able to return to their duties at one o'clock.

By means of this system, eastern New York state physicians have been keeping abreast of medical progress through the most natural medium, their medical school.

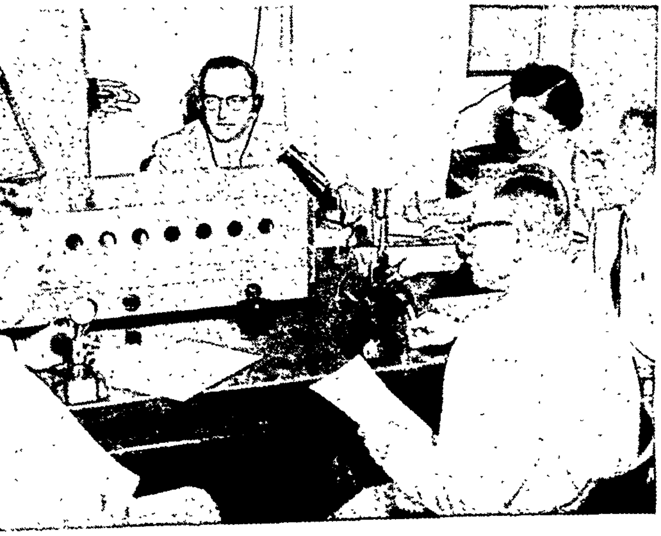
Postgraduate medical education by radio is the offspring of Dr. Frank M. Woolsey Jr., associate dean and director of postgraduate education at Albany. An amateur radio operator by avocation, Dr. Woolsey saw a chance to combine that interest with medicine when he came to Albany in 1954. The first network consisted of the medical school and three hospitals which happened to own amateur-operated transmitting and receiving equipment. When Dr. Woolsey switched his operations from short-wave to a noncommercial and relatively static-free FM frequency a little more than a year ago, his group had grown to include 21 hospitals with more than 75 amateur operators donating their time.

Outside Financial Aid

The work has been partly financed by grants from the Rockefeller Foundation which gave Albany $4,000 to begin its operations, and $90,000 for additional experimentation after its initial success. The current series is being sponsored in part by a grant-in-aid from E. R. Squibb & Sons. The basic plan is simple: Three times each week from November to May, two or three members of the Albany faculty go on the air with a 20-minute discussion of a subject chosen by a small committee of the medical college faculty. Ready and waiting at their own hospitals are physicians who have at their disposal transmitting and receiving equipment. As the faculty presentation ends, moderators transmit physicians' queries on specific points to the home station. Since there are usually eight hospitals participating in any given broadcast, they offer questions—two at a time—in rotation. Usually two complete circuits are made of the participating groups. Each hospital hears the questions asked by the other physicians and the answers broadcast by the faculty. Two similar broadcasts on the same topic are held during the same week to service the other hospitals on the network.

Dr. Woolsey's conferences have one big factor in their favor: they bring postgraduate education to the physician's doorstep, and thereby save him time, money, and effort. The fact that the doctor need give up nothing but his lunch hour probably accounts for some of their popularity.

But is it a satisfactory teaching method, this airwave classroom contact? Figures compiled for the first two years of operation show nearly 95% of the participating physicians rated the offerings



From Doctor to Doctor . .

Left, **faculty at Albany Medical College confer with staff of 23 hospitals via two-way FM radio. Clockwise from lower left are Harold C. Wiggers, Ph.D., dean; Albert Fredette, station manager; Miss Jeanne Roper, secretary; Dr. Frank M. Woolsey Jr., associate dean and director of postgraduate education; and Dr. William P. Nelson III, assistant dean and assistant director of postgraduate education.**

Wires and Wave Lengths

The use of two-way FM radio by the Albany Medical College is only one example of the profession's interest in electronic devices as aids in continuing medical education. Others include:

–Transatlantic telephone conferences between physicians in the U. S. and Great Britain at recent A. M. A. Annual and Clinical Meetings.

–Closed circuit color telecasts of surgical procedures and hospital rounds during the same meetings and in between, produced by pharmaceutical firms in cooperation with the A. M. A.

–A proposed open circuit series of telecasts on medical topics now being negotiated by a major broadcasting company and a pharmaceutical firm.

–A private circuit FM operation to carry news of medical advances and other postgraduate educational offerings to doctors' offices being planned now by another major network.

either "excellent" or "good" on opinion cards submitted after each session.

Other Schools Show Interest

Dr. Woolsey is a reluctant proselytizer for his new method. He says: "I do not want other schools to feel that they are being shoved in any way toward the possible development of two-way radio conference networks." But many of them have needed very little "shoving." Requests for information or visits by personnel have come from medical schools and hospitals in Pennsylvania, Kentucky, Massachusetts, California, and parts of Canada.

As in most experimental situations, the early days of Albany radio were not always smooth. On inquiry to the Federal Communications Commission in 1955, Dr. Woolsey was told that the amateur frequencies were the only ones available for the type of project he had in mind. Despite the inherent difficulties of trying to man any large number of transceivers with amateur operators on an inflexible schedule, this was accomplished and continued for two years. But by 1958, Dr. Woolsey, working with the FCC, developed a plan that utilized noncommercial FM frequencies and remote broadcast transmissions in a manner untried previously. He then proceeded to establish station WAMC with studios at the Albany Medical College and its antenna atop Mt. Greylock, the highest mountain in Western Massachusetts. The station has a 10,000 watt output and may be picked up by any FM receiver within 150 miles.

The cost of a radio system such as that used by Albany and its hospital network is not great. Dr. Woolsey estimates that a contribution of from $1,600 to $2,500 from each of 20 hospitals would be sufficient to pay for the purchase and installation of a system that would include a master transmitter at the medical school and remote pickup transceivers at each hospital.

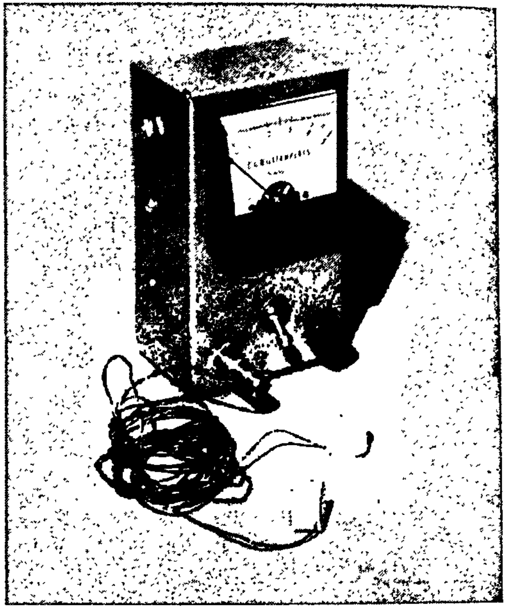
Postgraduate work by radio is not designed to replace intramural programs at the medical school, but rather to complement them. The subject matter of many of these courses, such as dermatology, precludes anything but personal attendance. Many others, however, lend themselves well to the radio technique supplemented if necessary by premailed mimeographed material.

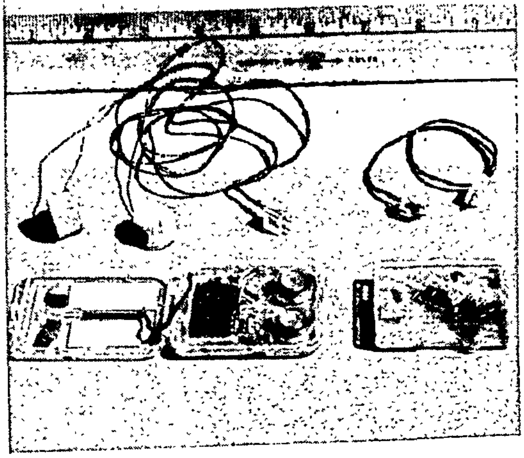
One of the initial qualms that accompanied the switch of Dr. Woolsey's system from shortwave to FM was the fact that using the FM band enlarged the potential audience from selected groups of doctors to any layman with an FM receiver. What would be the result if private citizens were exposed to lengthy discussions of diseases, conditions, symptoms, and treatment? Would such listening bring doubt and fear or would it send the listeners scurrying to their physicians with long lists of imaginary symptoms? No one knew for sure.

Experience with the Albany operation has shown no public inclination to take alarm from such broadcasts. Dr. Woolsey thinks this may be because laymen have found the discussions dull or unfathomable and therefore tedious. One New York physician has personal knowledge that at least one of his patients is a listener, however. The woman, who was recuperating, said she had listened to some of the programs and had been interested in the many questions asked by the participating physicians. She said: "It's nice to know that there are doctors who will admit they don't know everything."

. . Teacher to Practitioner

In hospital conference rooms, *right*, such as this one located at Vassar Brothers in Poughkeepsie, N. Y., physicians keep up with medical advances through the weekly radio series. During noon hour classroom time, they question faculty broadcasters by means of the transmitter in meeting room. Through network connection, they also hear other groups' questions.





Engineering and Medicine

How engineers work with physicians to attack specific health problems. *Upper left,* Dr. George V. LeRoy (in center) examines cytodiagnostic test apparatus for teaching laboratory technicians to recognize cancer cells. Punch card evaluates microscope slide. *Upper right,* electron stethoscope for quick visual and audible check. *Center left,* preliminary model of electronic calorimeter to measure changes in body heat. *Lower right above,* dime electrodes taped to chest, engineer demonstrates miniaturized heartbeat monitor to pathologist and telephone company president. *Bottom left,* close-up of same cumulative heartbeat recorder with amplifier. All devices are being developed by Illinois Bell Telephone Company engineers working during off hours in cooperation with University of Chicago medical researchers.

Togetherness in Heartbeat
Who Says Medicine and Engineering Don't Mix?

Two pathologists at the University of Chicago, Drs. Donald A. Rowley and Seymour Glagov, had a problem: How to keep accurate track of a person's heartbeats throughout a day or more without hampering his normal activities of work, play, and rest. This was no new question. Over the years many physicians have wondered about the relationship of pulse rates to circulatory diseases, smoking, body weight, occupational effort, maternal labor, sleep, athletics—to many aspects of persons in their environments.

Rowley and Glagov had one advantage over most of their colleagues, however. They could translate their problem into dramatic solution. And they did just that one day last month on the university campus when they displayed a 3-oz. device, comfortable and compact, that keeps a cumulative count of heartbeats. While the recorder (see photos on previous page) represents a significant medical advance in itself, even more important is the fact that it was produced in an atmosphere of liaison that signals growing cooperative efforts of physicians with practitioners of another discipline—engineering.

The relatively recent phenomenon of medicine at work with other arts and sciences has been noted previously as a powerful but still unsung force for progress in such fields as space exploration (Medicine at Work, THE JOURNAL, Jan. 31, 1959), basic research and medical education (Medicine at Work, THE JOURNAL, Dec. 21, 1957).

Those University of Chicago researchers, fortunately, had a catalyst in the person of William V. Kahler, a university trustee who also is president of the Illinois Bell Telephone Company. When medical faculty members posed some laboratory puzzlers, Kahler said: "Be specific. Tell me what you want, your immediate and most pressing needs."

Drs. Glagov and Rowley wanted a cumulative heartbeat recorder. Dr. George L. Wied of the department of obstetrics and gynecology wanted a cytodiagnostic test apparatus to help train exfoliative cytological technicians ("cancer detectives"). Dr. Klara J. Prec of the department of pediatrics wanted a tidal volume computer to help save newborn babies stricken with suffocating hyaline membrane disease. Mr. Donald Charleston of Argonne Cancer Research Hospital, which the university operates for the U. S. Atomic Energy Commission, wanted a special electronic circuit which could help pinpoint brain tumors.

The needs of these physicians are being fulfilled by nonphysicians—some 40 Illinois Bell Telephone Company engineers who belong to SAVE (Service Activities of Volunteer Engineers), a Chicago-area organization which is being groomed for national stature. Members welcomed the opportunity to exert individual initiative on their own time in garages, basements, and home workshops while serving medicine's goals to bring better health.

From Idea to Design to Product

Take the heartbeat recorder, for example. Engineers Leroy J. Ryan and Lou E. Harrington, given the medical problem, mapped out basic design and passed on the mechanics of construction to another telephone company employee, Watson B. McCreary, last September. McCreary, a watchmaker hobbyist for the past 15 years, picked up a $50 ladies wristwatch, removed the mainspring and hooked up the escapement mechanism of the modified timepiece to a pair of silver electrodes (dimes), some transistors, button-sized batteries, and a coiled magnet. In 90 days he created a gadget that ticks off the answers. The face of the "watch" does not tell time, of course. It is a form of adding machine. Modestly mass-produced, the precision device could sell to physicians for less than $200, according to Harrington.

Several weeks ago, Ryan linked it to a neon beeper in his living room and watched his five young children take turns "pasting on the dimes" so they could see and hear their own little heartbeats. Ryan himself kept a log:

"Saw the boss after work—113 beats per minute.

"Resting after kids to bed—86 bpm.

"Asleep—40 bpm.

"Fed baby before arising—61 bpm.

"Got up—65 bpm.

"Arrive work—102 bpm."

Harrington also kept a 24-hour log. One entry read: "Asked for raise—125 bpm."

"This invention is the equivalent of a $30,000 contribution to medical science," said Dr. Rowley. "But the patience, understanding, and willingness of these men to develop the instrument are invaluable. Dr. Glagov and myself hope they have enjoyed working in this cooperative project as much as we have."

Nobody is seeking a monopoly. All of the electronic circuits, as they become refined, are being made available to the medical profession. The research cost on all four projects to date totals only $400 for materials, with the university footing the bill. As far as Dr. Wied is concerned, such a cost is ridiculously low. Evaluating the cytodiagnostic test apparatus developed for him, he says: "The machine is priceless. It does not require me to stand behind each student to score each example. It gives me more time to devote to patients while

Discussion groups such as this at the Chicago conference hammered out recommendations on the expansion and improvement of homemaker services. Clockwise around the table are Miss Phyllis Osborn, Bureau of Public Assistance, Chicago; Miss Constance Hastings, Bureau of Public Assistance, New York; Mrs. Asher Yaguda, Newark; Dr. Marian R. Stanford, State Department of Health, Trenton, New Jersey; and Miss Margaret Gregg, State Department of Public Welfare, Austin, Texas.

still being able to train cytology technicians who are so badly needed."

"Medical Engineering"

The medical school as a whole, meanwhile, is sold on this kind of medical engineering—or engineering medicine, if you will—as a fitting key in research efforts. Dr. George V. LeRoy, professor of medicine and associate dean of the University of Chicago Division of Biological Sciences, says: "The present program of research cooperation with the members of SAVE is significant because it permits our clinical people to take advantage of a large store of information, the existence of which is either unknown to us, or to which we have limited access.

President Kahler of Illinois Bell is looking ahead, not only to more cooperative efforts of his fellow engineers with the medical researchers but to tapping a rich source of seasoned talent—the 195,000 active and retired telephone company workers who live in every region of the United States and Canada and who are ready to devote 20 or more years of individual know-how to supplement the community-serving activities of SAVE. They are called Telephone Pioneers, and Kahler is their international president. He says:

"This teamwork between dedicated and competent medical research doctors and telephone engineers is an outstanding example of public service. Their joint developments may be responsible for breakthroughs, which might otherwise have not been possible so soon, in the frontiers of biological science—and we know there will be more. Although we haven't come up with an electronic cure for the common cold—give us time—the advances to date demonstrate how two groups, with different professional backgrounds, can team up to solve problems for the common good."

Homemaker As One Prescription For Today's Troubled Family

HOMEMAKER, *n.* one whose occupation is household management.

The word denotes home operation, child rearing, and the creation of familial comfort. But Webster's definition could not have envisioned a different kind of homemaker—one emerging as a product of our modern times. The second definition includes all of the components of the first but with an important addition: she is available to take over when the family's usual "homemaker" is absent or incapacitated.

This second kind of homemaker was the one that interested some 400 persons who met in Chicago last month for the National Conference on Homemaker Services. Physicians, attorneys, social workers, insurance executives, labor representatives, nurses, industrial officials, and many others took part in the two-day session devoted to the exploration of ways to expand homemaker services.

A continuing interest in homemaker services has been expressed by the A. M. A. through committees of the Council on Medical Service. Dr. Philip S. Barba of Philadelphia, chairman of the Committee on Maternal and Child Care, acted as finance chairman for the Chicago conference. Section chairmen included Dr. Frederick Swartz of Lansing, Mich., chairman of the Committee on Aging, and Dr. Lemuel McGee, a member of the Council on Industrial Health.

A homemaker, under the definition used by this

One Family's Experience

A typical case for which the services of a homemaker were deemed a good solution to a family health problem is noted in an official report from Detroit:

"Mrs. M., the young mother of four children ranging in age from three to eight, was discharged from the hospital with a diagnosis of rheumatoid arthritis. Her children had been staying with relatives, and Mrs. M. was anxious to have them home with her. She could be up and around, but she was in pain, and her physician had ordered as much rest as possible. The Visiting Nurse Association helped with a plan in which a homemaker was assigned full time at first and then gradually reduced to one day a week. Mrs. M. did the meal planning, and the homemaker helped with the care of the children, cooking, light housework, and some ironing. As a result, the family was reunited and with rest Mrs. M. recovered. A total of 51 days of homemaker service were provided over a period of 19 weeks at a total cost of $612."

Persistence Succeeds in New Jersey

Much of the success in forming New Jersey's 13 homemaker services can be directly traced to the interest and persistence of two women—Mrs. Asher Yaguda, wife of a physician, and Mrs. Thomas F. Delaney, former executive director of the American Board of Pediatrics.

As members of the Essex County Service for the Chronically Ill in 1948, they conceived the idea of furnishing homemaker services to Essex County families who needed help. Their first attempts were to "sell" the idea to an agency which would implement it, but this they failed to do. Still undismayed, the two women then asked their own Service for the Chronically Ill to undertake the job despite the fact that the agency was specifically designed as a study group. With the backing of two physicians whom they had interested in the project, they got the agency's approval and set out to find some money to implement it. Their first donation—less than $300, most of which had to go for workmen's compensation and public liability insurance premiums—came from a woman's club in Newark, but it put them in operation.

An article in a Newark newspaper brought in 30 homemaker applicants, 10 of whom were accepted. These 10 were trained by experts loaned by the Red Cross, Public Service Company, and the Newark Health Department. The initial class was graduated in 1950, and got its first case soon after—a woman suffering from multiple sclerosis. Use of the service by the community was not immediate, however, and it took time to make the nature and value of the service known to physicians and welfare agencies in the county. Once the service became known, service requests boomed.

Medically oriented to the nth degree, Chr-Ill Service, as it is now known, requires physician approval for all referrals. The wisdom of the rule is indicated by the finding that 93% of all families served by homemakers in the U. S. during a "study week" in 1958 had members who were ill or disabled. Chr-Ill is sponsored by the Essex County Medical Society, and other New Jersey county societies and women's auxiliaries have been in the forefront of homemaker work in other areas.

All New Jersey services have medical advisory committees, and in at least one instance a physician was so impressed with the value of a homemaker on one of his cases that he paid for the service himself.

Success in Essex County turned out to be only the beginning. In 1953, the New Jersey legislature passed a prevention of chronic illness act which included a provision enabling the state health department to provide "housekeeping aid services." It also named a State Consultant Committee on Community Homemaker Services, and chose as its chairman an expert in the field—Mrs. Asher Yaguda.

group, is "a woman who is employed to help a family help itself rather than to provide domestic aid as it is generally understood." She is chosen, trained, paid, and supervised by an agency which assigns her to homes where help is needed, most often because of illness or incapacity. She is equipped to care for the needs of the children, perform routine household chores, provide meals, and do the marketing.

In days past, the help of mothers, sisters, and neighbors was often enlisted by families faced with difficulties, but the mobility of the modern family has frequently left it isolated from relatives and often with only a nodding acquaintance with neighbors. It is this social vacuum which the homemaker capably fills—to help keep family unity until crisis passes.

Beginnings and Adaptations

Although the first homemaker service was begun more than 30 years ago, only 150 of the nation's 3,100 counties have such a service available today, and in most of these the service is less than optimum. The Public Health Service reports 1,778 homemakers were employed in the U. S. in 1958 by 145 agencies. Three out of four (111) of the services are operated by voluntary agencies. Most of the remainder are programs of departments of public welfare.

Homemaker services were begun in different parts of the nation for different reasons, but all have a basic similarity:

—In New York City in 1933, the Homemaker Service of the Children's Aid Society was established as a joint experimental project with the Junior League. Its purpose was to come to the aid of distressed children by helping to care for them in their own homes in preference to boarding them out.

—Aid in family emergencies arising usually out of the illness or disability of the mother was offered by a homemaker service begun in 1940 by the Boston Provident Association. The work is now being continued by the Family Service Association.

—Homemaker service was begun in Cincinnati in 1930 when it was established with public funds as a WPA project. By the time public money was no longer available, the need for such a service was so obvious that it was taken over by the privately financed Family Service of Cincinnati and Hamilton County.

—New Jersey, where establishment and promotion of homemaker services has been widely endorsed by the state and county medical societies, has one of the best programs (see box). Indeed, its 11 autonomous homemaker services, with the aid of the state health department, have trained 575 homemakers, a figure which equals nearly one-third of the national total reported in a 1958 survey.

—In 1937, an attempt at providing homemaker service for rural areas was begun by the Colorado State Department of Public Welfare.

Criteria for Assignment

Homemaker services vary in the conditions under which they will assign workers to homes. Many concentrate on families where children will be directly affected; some are occupied with the problems of families faced with chronic illness; others attempt to serve any obvious need. The problem of payment by the recipient is met in many ways too. Usually those who are able to make their own payments do so directly to the agency. In other cases, they may make payments according to their ability based on a sliding fee scale. Homemaker services are sometimes purchased for recipients by welfare agencies.

Judging by the results of the Chicago conference, there is work ahead for those promoting homemaker services. Recommendations of the study groups which explored all phases of the future showed there is a need for:

—Broader understanding and support, especially from the groups which benefit indirectly such as industry and labor.

—The development of new methods for the establishment of homemaker services, particularly in rural areas.

—Study and evaluation of the existent variations in homemaker service programs.

—Provision for adequate money to meet the financial needs of the families served by homemakers.

—Clarification of policies of national voluntary agencies with regard to the role the local affiliate should take in participating in the organization of services.

One of the most valuable by-products of homemaker services is the opportunity they afford to mature women, many of them widows, to continue to play an important role in the community and to earn some money at the same time. Although the hourly wage of the average homemaker hovers near $1.25, the work apparently pays off in other ways. A visitor to one agency was introduced to an elderly lady identified as "one of our homemakers." She carried a book and, when the visitor asked what it was, she proudly displayed its title—"The Joy of Cooking."

A. M. A. Committee's Relative Value Study

The A. M. A. Committee on Medical Practices is now preparing its first publication to help state societies desiring to make relative value studies similar to those done in California, Kansas, and Iowa. The series of publications will include general information bulletins and survey manuals. These will be offered for inspection and comment at a series of regional meetings, the first of which will be held in San Francisco next month.

According to a Committee report to the House of Delegates last December, relative value studies may be used for several purposes but their chief value will be to enable health insurance and prepayment plans to set up benefit schedules that "bear a more constant relationship percentage-wise to the actual, usual or customary fees of physicians."

The Delegates agreed, called upon the constituent associations to consider the conduct of such studies, and directed that the Committee help them.

The stated purpose of a relative value study is to show—by some numerical designation other than money value—relationships between time, competence, effort, expense, and other factors required to perform one professional service as compared with those required for other professional services. Relative value studies are not fee schedules but may be the basis for developing realistic schedules of allowances.

Simply stated, the relative value study includes

Arguments Against Relative Value

What about the other side of the coin? Is there a case against relative value studies? Some physicians believe there is and have said so.

Perhaps their greatest objection is that, although the relative value principle makes only unit relationships between procedures, in practice this purpose could be subverted by those who might apply a set of dollar values to the scale, and then cry out against any deviation.

Another objection, voiced by at least one specialty group, is that proposed relative value studies do not adequately differentiate between procedures performed by a board-certified specialist as against the same procedures done by a physician without a specialty certification.

One objector bases his criticism on the fact that a given procedure with a set unit value on the schedule may in fact take much more time in one case than in another. Dr. Arnoldus Goudsmit of Youngstown, Ohio, writing in a national publication, uses that thesis to argue against relative values. As an alternative, he suggests that each physician determine his hourly rate and set fees according to the time given to the patient.

A Relative Value Sample in California

How might you use a relative value study in setting your own fee schedule? It can be easy, according to information published for the use of California physicians who wanted to do just that:

Once the physician receives his copy of the relative value scale, he has only to use the dollar value of some fundamental service in his practice—such as a follow-up office visit—and apply it as a basis for computing his normal fees for the other procedures listed in the scale. Such calculations need be made only once, and then kept for referral purposes.

But for those mathematically inclined, the California report explains it this way:

"If you normally charge $4 for follow-up office visits (Procedure Code No. 006 in the California study) which has a relative value of 35, how much should your fee be for a first home visit (003) which has a relative value of 70? Use this formula: $4 is to 35 as X is to 70. Multiply $4 by 70, which is $280; divide by 35 and your answer is $8—or the dollar value of the first home visit.

"You can establish your own conversion factor. Four dollars for a follow-up visit is approximately 11.42% of 35, its relative value. Take 11.42% of the relative value of each procedure, and you will have a fee schedule with correct values based on a $4 follow-up office call."

two elements:

—A comprehensive survey of the relationships between the usual charges made by members of the constituent association for professional services.

—A statistical evaluation resulting in the assignment of a unit value for the various procedures.

The California Medical Association's pioneering study was adopted in 1956 after three years of committee work. It was updated and republished in late 1957, and is currently being revised. It has been used by both Kansas and Iowa as a model for their own studies. The relative value study as adopted in California is subdivided into four parts and contains separate schedules for medical services, surgery, radiology, and pathology.

In urging constituent associations to undertake studies of their own, the House of Delegates suggested "using the nomenclature, descriptions and code numbers of the California study to avoid confusion." In its report to the House, the Committee stated:

"Unless studies of this type are made in the near future and adopted by the medical profession, medicine runs the risk of alienating public opinion and losing its bargaining position with other agencies engaged in financing the cost of medical care. If medicine does not undertake this activity, it may be done by others who are much less qualified."

Dr. Lester D. Bibler of Indianapolis is chairman of the House of Delegates Committee on Medical Practices. Other members are Drs. James P. Hammond of Bennington, Vt.; Elmer G. Shelley of North East, Pa.; J. S. DeTar of Milan, Mich.; and James M. Kolb of Clarksville, Ark. Mr. George W. Cooley of Chicago is Staff Secretary.

Accentuating the Additive

Today, in some rural communities, you still find those who salt their own meat. In using salt as a preservative, they are practicing an art, the origins of which are lost in antiquity. But they are also using an "additive" under modern definition, and food additives are very much a modern subject.

This month, an amendment to the federal Food, Drug, and Cosmetic Act went into effect. Its major provisions (which won't be totally effective for 30 months) will be to make the manufacturer of any food additive responsible for proving his product is harmless to human beings. In the past, a chemical used as a food additive had to be proved unsafe before it could be excluded from grocers' shelves by court action.

Under the new regulations, the manufacturer must make acute, subacute, and chronic oral toxicity tests using laboratory animals and submit the findings to the Food and Drug Administration which will regulate the quantities and usages.

Increased emphasis on the intermediary contract for hometown care of veterans with service-connected disabilities and efforts toward a return to the original principles of Medicare were discussed last month by the A. M. A. Committee on Federal Medical Services meeting in Chicago. Chairman of the group is Dr. Russell B. Roth (head of table) of Erie, Pa.

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NAMING OF DRUGS ON PRESCRIPTION LABELS

UNLESS DISPENSED in original containers which have undetachable labels, most prescription labels bear only the name and address of the pharmacy, its prescription file number, the names of the patient and physician, and the latter's directions for use. The absence of any display of the name of the prescribed drug or drugs appears to be a matter of custom although intentional secrecy has been largely superseded by the use of English for writing prescriptions. Indeed, physicians frequently tell patients the name and nature of prescribed drugs unless there is a particular reason for withholding this information. Mutual confidence between physician and patient is likely to be enhanced by the plain designation of the principal ingredient(s) on the prescription label. The directions for administration are often too complex and varied to be encompassed on a small label; in some cases the warning to take only as directed may be the most useful inscription.

Identification of prescribed medication on prescription labels also may aid physicians other than the prescriber, as well as dentists, who may be consulted for the same or for a different ailment. Even the original prescriber may be unable to recall or find a record of the precise medication prescribed for a patient whom he has not examined recently. Moreover, the identification of a prescribed drug may be urgent in emergencies which involve a question of accidental poisoning, unintentional overdosage, or attempted suicide. Determination or confirmation of the exact identity of a previously prescribed drug in such cases may be hampered by the necessity for calling or contacting the dispensing pharmacy to obtain the information from the number of the prescription in its files. Such occasions, arising after closing hours, would involve even greater loss of time. There also may be other more or less urgent situations in which a clinic or private patient is obliged to consult or call an alternate physician for refill of a prescription, the identity of which can be determined only by contacting the office of the prescriber or the dispensing pharmacy. Indeed, on account of travel or changes of residence, patients may be put to extra expense because the identity and suitability of partly used prescriptions cannot be determined by another physician.

While display of the names of prescribed drugs on prescription labels can be advantageous, there are some patients for whom it may be unwise to reveal such information. These might include patients with mental disturbances, diseases known to have a fatal outcome, or any condition likely to be aggravated by a knowledge of its consequences, particularly if the name of the particular drug prescribed has a specific connection with the diagnosis. In such cases names which are therapeutically suggestive would be especially provocative. Another unfortunate aspect of prescription drug identification lies in the encouragement it may provide for sharing unused medication with another member of the household or a neighbor who has or is assumed to have the same illness. Because of wrong diagnosis, different stage of illness, or different dosage requirement, this could easily lead to serious consequences.

Although this is a delicate matter which should be left to the judgment of the physician in each individual case, it is suggested that with a somewhat larger section of the public than in former days the naming of drugs on prescription labels will work for good rather than for harm.

ANNUAL A. M. A. MEETING IN ATLANTIC CITY

Now is the time to make your hotel reservation for the annual A. M. A. meeting in Atlantic City which opens on June 8 and continues through June 12. The advance registration form and the hotel registration form appeared in the February 14 issue of THE JOURNAL, page 224.

Atlantic City has expanded its housing accommodations since the Association last met there. Nearly 5,000 new motel accommodations have been constructed within the city limits. Many of the motels are on or near the boardwalk. You are assured the widest selection of housing accommodations if you make your reservation now. A map showing the locations of the hotels and motels also appears on page 224 of the February 14 issue of THE JOURNAL.

ORGANIZATION SECTION

NEW COMMITTEE ON HYPNOSIS

At its meeting Feb. 6 and 7 the Board of Trustees voted to approve the establishment by the Council on Mental Health of a Committee on the Medical Use of Hypnosis. The Committee is composed of Drs. Harold Rosen, Baltimore, Chairman; Zigmond M. Lebensohn, Washington, D. C.; and Louis J. West, Oklahoma City. The date for the first meeting of this Committee has not, as yet, been set. The Committee will concern itself chiefly with the problem of implementing the suggestions and ideas expressed in the Council's report on the medical use of hypnosis, which was approved by the Board of Trustees and the House of Delegates of the American Medical Association and published in full in The Journal (Sept. 13, 1958, pages 186-189). The Board emphasized that the notice published in The Journal (Jan. 3, 1959, page 54) concerning the American Board of Medical Hypnosis in no way indicates that this "Board," which presumably has set itself up to serve as a certifying body for physicians using hypnosis, is connected with or approved by the American Medical Association or its Council on Mental Health. It is believed that two or three such groups have been set up in the United States. They seemingly allege in their announcements that they are functioning in collaboration with the Association or with the Council on Mental Health which definitely is not so. The general, and as yet unofficial, opinion of our Council's newly formed Committee on Hypnosis is that hypnosis itself has so far not advanced to the point where it can be considered to be a specialty apart from other medical specialties or apart from medicine in general. Dr. Harold Rosen, 1101 N. Calvert St., Baltimore 2, Chairman of the A. M. A. Committee, will be pleased to answer inquiries concerning problems of training in the use of hypnosis in practice from individual physicians and members of the Association.

PESTICIDES BOOKLET

A 64-page booklet, "Open Door to Plenty," is now available free of charge to A. M. A. members and others interested in learning how pesticides are used to protect food, property, and health. The easily read booklet is described as "an excellent summary of basic information" by the A. M. A. Committee on Pesticides, which makes a continuing study of precautions that should be followed for the safe handling and use of pesticides. Copies may be obtained by writing to the Committee at A. M. A. headquarters or to the publisher, the National Agricultural Chemicals Association, 1145 19th St. N. W., Washington 6, D. C.

FUNDS FOR MEDICAL SCHOOLS

A total of $4,133,839 was given to medical schools during the 55th Annual Congress on Medical Education and Licensure in Chicago, Feb. 9, by the National Fund for Medical Education and the American Medical Education Foundation. Dr. John McK. Mitchell, president of the Association of American Medical Colleges, accepted a check for $3,000,185 from Chase Mellen Jr., executive vice-president of the National Fund, and another $1,133,654 from Dr. George F. Lull, AMEF president. (See Medicine At Work in this issue for report on the Congress.)

CONFERENCE ON PHYSICIANS AND SCHOOLS

The seventh National Conference on Physicians and Schools will be held Oct. 13-15 at the Moraine-on-the-Lake Hotel, Highland Park, Ill. It is sponsored by the A. M. A.'s Bureau of Health Education. The conference is restricted to officially delegated representatives of state and territorial medical societies and health and education departments. More than 200 persons are expected to attend.

REVIEWS OF MEDICAL MOTION PICTURES AVAILABLE

The 10th annual publication of "Reviews of Medical Motion Pictures" is now available on request from the Film Library of the A. M. A. This publication is prepared by the Division of Communications, Department of Medical Motion Pictures and Television, and contains reprints of all reviews published in The Journal during 1958.

COUNCIL ON INDUSTRIAL HEALTH

PREVENTION AND CONTROL OF OCCUPATIONAL DERMATOSES

This is the last in a series of five reports prepared by the Committee on Occupational Dermatoses of the Council on Industrial Health, American Medical Association.

B. Dixon Holland, M.D., *Secretary.*

Occupational dermatoses cost this nation millions of dollars in lost time, lessened efficiency and production, and medical care and compensation each year. There are no figures which relate accurately the total cost of these diseases, but the money spent for medical care and compensation is admittedly excessive. These facts become more important when it is realized that occupational dermatoses are, in large measure, preventable.[1] Because of the continued prevalence of these diseases and the inconvenience and suffering which accompany them the Committee on Occupational Dermatoses has seen fit to review the measures which can be used to prevent and control occupational skin diseases.

The prime requisite in preventing occupational diseases in general and dermatoses in particular is cleanliness. Unless the workman, his clothing, his machine, and his working environment are kept clean there can be no control of skin diseases in industry. These essentials are attainable, for it is now generally accepted that appropriate engineering methods can control a noxious environment, and medical methods can do much to control the hygienic practices of the workmen.[2] For many years, large plants have been aware of the importance of providing a safe working place. The modern plant attains this by good construction, the installation of automatic equipment, and the use of closed process systems which protect the workman from harmful materials with which he must work. The basic chemicals can be transported to the plant in sealed cars, emptied into closed storage areas, and then piped into totally enclosed chemical reactor systems. Of course, this method of handling cannot be used in all plants because some processes do not lend themselves to closed systems or perhaps in certain plants the closed process may prove too expensive. With less cost, good ventilating systems to collect toxic materials can be used to control the spread of irritant vapors, fumes, mists, and dusts.[3] Competent guidance can be obtained from private consultants, universities, many of the state health departments, and some of t state labor departments who offer consultati services on industrial hygiene engineering pro lems.

Where good engineering devices are used to co trol the environment, occupational dermatoses a less prevalent. However, at the present time it estimated that less than one-third of the worki population has access to good environmental co trols within the plant. As a result, small plants wi poor environmental hygiene contribute heavily the sustained prevalence of occupational skin d ease.[3]

Responsibilities of Medical Department

Large plants rely heavily on their medical d partments to prevent occupational diseases. Co trols, including personal hygiene, are the respo sibility of the medical, industrial hygiene, nursin and safety personnel. Over the years, hygien practices have improved, and at this time a go medical department generally assumes the follo ing responsibilities directed at preventing occup tional skin diseases.

Education.—The first step in setting up a go educational program directed at preventing occ pational skin disease takes place when the medic industrial hygiene, safety, supervisory, and pr duction personnel develop a thorough understan ing of the existing hazards within the plant. This done by conducting a complete survey of all pla operations and observing the men at work so th the potential health hazards can be determine Once this appraisal of the hazards within the pla has been made, management, superintenden foremen, and old as well as new workmen shou be instructed about the hazards and the measu which must be taken by the men to avoid occup tional illness and injury. In plants where workm are not informed of the existing hazards, occup tional dermatoses are common. The physician w treats occupational dermatoses should visit t plants where the cases arise. Much can be learn about the causative factors which produce occ pational dermatitis, but, even more important, t physician can develop a practical attitude concer ing preventive measures.[4]

The members of the Committee on Occupational Dermatoses are Drs. Donald J. Birmingham (Chairman), Cincinnati; Leonard Weber, Chicago; Frank C. Combes, New York; A. Fletcher Hall, Santa Monica, Calif.; James W. Jordan, Buffalo; George Morris, Boston; and Ray O. Noojin, Birmingham, Ala.

Medical Preventive and Control Measures.—The intelligent use of the preplacement physical examination can do much to prevent occupational disease. Today, the preplacement physical examination is used to better define job assignments within the limits of a worker's mental and physical capacities. As with other systems, the skin is important in the preplacement physical examination, because thorough observation can lead to the detection of those abnormalities which are likely to be aggravated by the working environment. Practical application of this fact can be seen in a few examples. Young people with acne vulgaris have a predisposition for developing occupational acne from tars, pitches, certain chlorinated hydrocarbons, and, most of all, cutting fluids.[5] Individuals suffering from psoriasis or lichen planus can experience severe aggravation of their disease because of chemical or physical injuries to affected or unaffected parts of the skin.[5] The keloid formation tendency among certain members of the dark-skinned races provides another example. Rosacea becomes worse when workmen having this disease are exposed to heat or to the vapors of alcohol. Seborrheic dermatitis can be exacerbated by contact with oils and greases. The atopic skin, well known for its unpredictable behavior, can be adversely influenced by dusts, solvents, exposures to grease, and temperature and humidity changes.[6] These dermatological facts can be of infinite value to the alert examining physician in the preplacement examination and in the management of the employee at work.

At times, it is not possible to prevent completely the occurrence of occupational dermatoses. It then becomes highly important that the physician be able to control isolated cases or outbreaks of skin disease which are occurring within the plant. This cannot be done, however, unless the physician is able to recognize the cutaneous disease as being of occupational origin and then to identify the causative agent. When recognition of the disease and its cause can be done promptly, the attack of dermatitis will be minimized and the man can generally continue to work by using proper protective devices. It is utterly impossible to control dermatoses of contact origin if the cause has not been detected and the patient is permitted to undergo continued exposures.

Personal Cleanliness.—Personal cleanliness is invaluable in preventing occupational skin disease. Industrial ventilation systems and good housekeeping are important in maintaining a clean environment, but there is no substitute for washing the hands, wearing clean clothes, and keeping clean. The basic necessities for the maintenance of personal cleanliness are the washing facilities and the proper skin cleansing materials. They must be adequate in number for the men who will use them, well designed, maintained in continuous working order, and, of no small importance, they must be conveniently located. If a workman must walk long distances in order to wash he generally will do so infrequently.[7] The type of cleansing material to be used should be selected for the job whenever possible. The number of times workmen must wash during the work shift will depend on the nature of the material being handled, but most workmen generally wash at least three times a day, for example, during the morning, before lunch, and again at the close of the shift. If the work soil is heavy, the workmen may find it necessary to wash many times during the course of the day. Skin cleansing is highly dependent on the type of industrial hand cleansers used, because removal of irritants and sensitizers from the skin must be thorough to prevent prolonged contact which leads to dermatitis. However, the frequent or even the infrequent use of harsh or poor quality skin cleansers may cause dermatitis, especially in those workers with dry skin or among those who work with solvents, alkali, and other materials that cause dehydration and removal of lipid.[8] Industrial cleansers include a wide variety of soap and related compounds in the form of plain soap powders, abrasive powders, abrasive cakes, liquids, and the so-called waterless hand cleaners. There are several well-known, time-tested industrial cleansers made by reliable producers. Powdered conventional soaps are usually satisfactory for the removal of heavy soil from the skin. In some of these powdered cleansers or cake cleansers, finely ground sand, pumice, powdered wood chips, and ground corn cobs, among other abrasives, have been added to the soap to effect better removal of the soil. Occasionally, this type of abrasiveness may overcome any mildness which is present in the soap. Corn meal and wood flour are considered efficient and acceptable abrasive additives.

Many of the cleansing agents also contain wetting agents, water softeners, and chelating agents. These improve the detergency of the soap, but they can also increase the potential irritant properties of the products, particularly if their continued use causes an increase in the pH of the skin.

Sulfonated oil soaps and other acidic skin cleansers (pH range of 7 or less) are good for cleansing the skin when soilage is less severe and easily removed. Schwartz and others [9] have found liquid sulfonated oils (soapless soaps) to be excellent cleansers for the removal of cutting fluids and even more tenacious soils. A distinct advantage of the sulfonated oil is that it can be used with less irritation to the inflamed skin by workmen with mild dermatoses.

Within the past few years, germicides, notably hexachlorophene and, more recently, tetramethylthiuram disulfide, have been added to soaps to increase their antibacterial power. Several industrial cleansers contain hexachlorophene and these can be used to advantage by food handlers, meat packers, and by those who have other exposures where bacteria play a primary role in causing occupational dermatitis.

Lanolin is a common additive to many industrial soaps. There is some controversy as to whether or not its presence is necessary, but it is believed that lanolin does tend to buffer the lipid-removing and dehydrating actions of soaps on the skin.

A group of products which have attained a renewed popularity are the waterless hand cleansers. These preparations are usually semisolid cream or paste or liquid materials which cleanse the skin without requiring use of water. They exert their action on the skin either by their wetting agent content or by solvent action, or by a combination of solvents and alkalis. Most of the waterless hand cleansers remove oils, greases, grimes, and paints, with other heavy soilage from the skin, quite satisfactorily. This advantage provides a selective utility for removing certain soils which ordinary soaps fail to dislodge completely. A good waterless hand cleanser can replace effectively raw solvents so commonly used for hand cleaning purposes. They have a definite application in operations where machinists, mechanics, field crews, road gangs, and maintenance men must walk long distances to obtain washing facilities. Several of these products are considered acceptable for use and have been on the market for at least five years, but waterless cleansers do not constitute a replacement for soap and water in all jobs.[10]

A few years ago, Dr. Louis Schwartz,[7] in a publication entitled "The Prevention of Occupational Skin Diseases," written for the Association of American Soap and Glycerine Producers, Inc., suggested the following basic requirements in selecting industrial skin cleansers, which, if followed, will generally lead to the choice of a satisfactory one:

1. They should quickly and efficiently remove industrial soil.
2. They should not harmfully defat the skin by normal application.
3. They should not be unpleasant to use.
4. They should not abrade the skin.
5. They should not be strong skin sensitizers.
6. They should flow easily through dispensers.
7. They should not become insect infested under normal storage conditions.
8. They should not clog the plumbing.

The industrial physician, safety director, or the consulting dermatologist should be able to select an industrial cleanser which is not harmful to the normal skin and which at the same time will remo efficiently the soils encountered. This is not a dif cult task if the one selecting the cleanser und stands the basic essentials concerning the action soaps on the skin, and, in addition, has some miliarity with the well-known products availal for purchase.[11] Considerable information along tl line can be obtained by referring to the abo mentioned work by Schwartz.

Protective Clothing.—In some plant operatio the workman finds it impossible to keep his clo ing clean no matter how carefully he handles t materials with which he must work. Work clothi laden with irritant or allergenic chemicals can p duce dermatitis. Similarly, oil-saturated shi trousers, or shoes induce comedones, erythen and dryness of the skin, and eventually occu tional acne.

Present-day protective garments are both attr tive and useful. They can be made from rubb leather, cotton, or synthetic fibers. Some of the n fabrics will protect specifically against acids alkalis, others against extreme degrees of he cold, or moisture. In highly hazardous operatio it is common practice for plants to furnish workmen with protective clothing. When clothi is furnished by management, there is better cont over the wearing, laundering, and servicing of garments. In addition, this practice insures agai the hazard of laundering the family clothing w noxious chemicals contained in the work cloth In plants where a workman must furnish his o protective clothing, there is little or no control o the type of protection furnished and not inf quently the prevalence of dermatitis cannot lowered. Some operations require the wearing impervious gloves and/or sleeves; however, recommending these devices, knowledge of operation in which the sleeves or gloves are to worn is essential. For example, a protective slee or glove worn near moving machinery could be cause of a serious accident. We have found tl surgical stockinet sleeves and cotton gloves protect the hands, wrists, and forearms agai moderate dust exposures. These materials are expensive; they are not cumbersome; and, by is ing two or three pairs of gloves and sleeves perio cally, they can be changed as often as necessa

Aprons can be obtained in fabric or plastic n terials. They have special value in protecting body against cutting fluids. The apron shou cover most of the chest and extend below knees. If the apron is to be an effective protecti however, it must be cleansed daily.

Protective gloves can be made of leather, natu rubber, synthetic rubber, or plastic material. T seams should be smooth to avoid trauma wh wearing. When gloves are worn to protect the hands against irritant chemicals they should cover most of the forearm, and the cuff should fit under an impervious sleeve which fastens at the wrist. This prevents the entrance of chemicals into the glove cuff.

Rubber gloves are an essential protective device in certain exposures to chemicals. Before recommending them, however, the nature of the exposure should be ascertained, because natural latex rubber gloves will not protect adequately against oils or chlorinated hydrocarbons. For these exposures, synthetic rubber or neoprene-dipped gloves must be worn. On occasion, the wearing of rubber gloves may produce eczematous-like lesions of the hands in those individuals whose perspiration is excessive. To combat the latter problem, and to provide greater comfort for all workmen who must wear rubber gloves, it has become common practice to advocate individual cotton liners underneath the rubber gloves. These can be changed as often as necessary.

Where potent skin sensitizers are encountered and the incidence of dermatitis without protection is high, it may be necessary to institute a more formal "protective clothing program." Educational elements to stimulate motivation and understanding and specific and detailed instruction in the use of protective clothing are essential. In some instances, regular and frequent inspection of the hands and arms by the nurse or the supervisor has facilitated the early identification of dermatitis.

A word of caution concerning protective clothing is given to the plant physician as well as to the consultant who on occasion can be misled by the workman who claims that he always wears protective clothing, including gloves. A few moments spent in examining the gloves or other garments may save considerable time in making a diagnosis, since wearing of clothing or gloves impregnated with irritant or sensitizing chemicals makes it impossible to avoid cutaneous contact with these materials.

Barrier Creams.—Barrier creams, or protective ointments, are popular with workmen, but these materials do not provide the degree of protection afforded by properly designed and maintained protective clothing. Notwithstanding, there are instances in which these preparations can be used to great advantage. Such is particularly true in occupations where wearing a face shield would be too cumbersome, or where skilled workmen cannot wear rubber gloves because of interference with the sense of touch. Well-instructed workmen understand clearly that a barrier cream, to be effective, must be applied to the skin before beginning work, washed off before lunch, reapplied after lunch, and again removed at the close of the workday. If the areas to be protected become soiled in between these periods, it may be necessary to remove and reapply additional barrier agent. In those plants where the program of occupational health is poor or absent, the workmen, through lack of instruction, generally do not understand the need for this routine. As a result, they sometimes develop a false sense of security with respect to barrier creams. Indeed, it is not uncommon to find workmen treating their cases of dermatitis with the barrier agents designed to prevent the eruption. Basically there are three types of protective or barrier creams: 1. The simple vanishing cream, or the invisible glove type cream, which fills the pores to prevent the entrance of irritants. Because of the formula, soil is easily removed along with the barrier cream on washing after work. 2. The water-repellent type which permits the formation of a film of water-repellent substance such as lanolin, beeswax, petrolatum, or silicone on the skin to prevent contact with water-soluble irritants such as acids and alkalis.[12] 3. The oil-repellent and solvent-repellent type which depends on water-soluble gums such as acacia, tragacanth, methyl cellulose, or moss gel to repel oils and solvents.

At this time, there is no all-purpose barrier cream which protects against all materials handled at work. For this reason, considerable thought must be given to the type of barrier cream prescribed. It is a waste of money and time to have the workman or the patient use a water-repellent cream when he is also exposed to solvents or light oils.

Conclusions

The majority of occupational dermatoses can be prevented by maintaining a clean working environment, but where environmental control is poor the most essential factor is maintaining cleanliness of the skin and the clothing. Workmen must be taught the importance of cleanliness and furnished with the necessary facilities to keep clean. Where possible, protective clothing and barrier creams should be used to support personal cleanliness. If these basic rules are not recognized by management and followed by the workmen, occupational dermatitis is inevitable.

Failure by the attending physician to appreciate these basic necessities frequently leads to protracted cases of occupational dermatitis. The therapeutic approach in the management of these diseases can be appropriate and rewarding, but it will prove fruitless unless the physician recognizes fully the significance of the contact factor in the plant and directs his major effort toward preventing further contact.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

POSTGRADUATE COURSES FOR PHYSICIANS

Notice of the following postgraduate courses for physicians has come to the attention of the Council on Medical Education and Hospitals since the publication of its annual list in The Journal, Aug. 16, 1958, for the year beginning Sept. 1, 1958. Each year a greater proportion of postgraduate courses are planned sufficiently in advance to be included in the annual listing, which provides a central reference more likely to bring courses to the attention of potential physician enrollees than can supplementary notices. Considering that more than 90% of the courses that eventually come to the attention of the Council are now included in the annual listing, it is expected that it will be possible to include all of the courses for the year beginning Sept. 1, 1959, in the annual listing, without supplementary notices. However, bringing the following information that has come in to the Council office to the attention of the profession appears desirable at this time.

The Medical Division of the Oak Ridge Institute of Nuclear Studies will conduct the second week of a pre-clinical course in **radioisotope methodology** for physicians April 27-May 1, 1959. The first week of this course was presented in February. Participants should have a basic familiarity with the techniques of using radioisotopes in medicine. The course will be repeated beginning June 1. Another three-day course in **thyroid measurements** will begin on July 6, to be followed July 9-10 by its clinical applications. Each course utilizes lectures, laboratory work, demonstration, audiovisual aids, open question periods, with the enrollee performing procedures. The fee for each course is $25. Requests for application blanks and further information should be directed to Mr. William B. Jones, Medical Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

The Department of Postgraduate Medicine of the University of Michigan Medical Center, University Hospital, Room 1610, Ann Arbor, Mich., can arrange tutorial clinical instruction in the **clinical use of radioactive isotopes** to aid the physician to qualify for use of radioactive isotopes in practice. Training is offered to one to four physicians at a time, licensed to practice medicine, who are usually certified specialists in radiology, internal medicine, surgery, or clinical pathology. Training is given simultaneously to residents in the hospital in these fields. The tuition is $50 per week.

A **Pediatric Symposium** will be presented on March 26-28, 1959, at the Auditorium, Texas Children's Hospital, Houston. Subjects will include staphylococcic disease, the neonate, infectious diarrhea in infancy, bone dysplasias, and diagnostic problems. For further information, address Dr. Russell J. Blattner, Department of Pediatrics, Baylor University College of Medicine, Texas Medical Center, Houston.

March 27-29, a postgraduate course in **congenital heart disease** will be presented at Grady Memorial Hospital, Emory University School of Medicine, 69 Butler St., S. E., Atlanta 3, Ga., at a fee of $50. For further information, write to Postgraduate Education at the above address.

The Twelfth Annual **Cancer Symposium** will be held March 31-April 1 at the Indiana University School of Medicine, Indianapolis 7. It will be devoted to the recognition and definitive management of neoplasms of the nose, paranasal sinuses, pharynx, larynx, the salivary glands, and regional metastases from these sites. There is no fee.

A one-day course on the **treatment of heart disease** will be presented April 29 at the Indiana University School of Medicine, devoted to the recent advances in the medical treatment of the various phases of heart disease. The fee will be $10. The following day, April 30, there will be a brief course on the **treatment of hypertension** to present the recent advances in the medical treatment of various hypertensive states. The fee will be $10. For further information, address the Director of Postgraduate Medical Education, Indiana University School of Medicine, Indianapolis 7.

The American College of Chest Physicians, 112 E. Chestnut St., Chicago 11, will present the Twelfth Annual Postgraduate Course on **Diseases of the Chest** for physicians in general and part-time specialty practice, at the Sheraton Hotel in Philadelphia, March 30-April 3 at a fee of $75 for college members and $100 for nonmembers. The methods of education will include lectures, panel discussions, open question periods, and audiovisual aids.

A one-day nine-hour course on **common neurological disorders for the general practitioner** will be presented April 15, 1959, at the Statler Hotel, Los Angeles, by the American Academy of Neurology. Educational methods will include laboratory work, seminar, lecture, panel discussion, open question periods, and audiovisual aids. The fee will be $10.

A course entitled **Topics in Clinical Medicine** will be presented May 11-16 at the Johns Hopkins Hospital, Baltimore 5. This five-and-one-half-day course is designed for physicians primarily interested in internal medicine. Registration will be limited to 150 physicians, at a fee of $100 each. Further information should be obtained from Dr. Philip A. Tumulty, Chairman, Postgraduate Committee.

A three-day course in **neurology** will be presented May 14-16 at the University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20. Further information should be obtained from the office of Postgraduate Medical Education at the school. That school will also present a course in **ophthalmology** on July 6-9 at Aspen, Colo.

The Eighth Annual **Postgraduate Seminar for Pediatricians** will be held at St. Christopher's Hospital for Children, 2600 N. Lawrence St., Philadelphia 33, May 20-23. This four-day 25-hour course for full-time specialists will include as educational methods patient demonstration, live clinic, bedside rounds, clinical conference, seminar, lecture, panel discussion, open question periods, and audiovisual aids. The fee will be $75. Further information may be obtained from the Professor of Pediatrics, Temple University School of Medicine, 3400 N. Broad St., Philadelphia 40.

The **Fourth Annual Postgraduate Course in Fractures and Other Trauma** for full-time specialists will occur June 8-13 at Cornell University Medical College, 1300 York Ave., New York City 21. The six-day 44-hour course will include as educational methods, clinical conference, seminar, lecture, panel discussion, and question periods. The fee will be $150. For further information address Dr. Preston A. Wade at the Medical School.

During the week beginning June 15, 1959, the **Second Annual Refresher Course in Diagnostic Roentgenology** will be held at the Cincinnati General Hospital, Cincinnati 29. The course will present various aspects of diagnostic roentgenology with emphasis on fundamentals. Enrollment is limited to radiologists and radiology residents, at a tuition fee of $150. Further information may be obtained from Dr. Benjamin Felson, X-Ray Department of the Hospital.

From June 18 through Aug. 1, 1959, the University of Michigan School of Public Health, Ann Arbor, will present a course in **health statistics.** Further information may be obtained from the Director, Summer Program on Statistics in the Health Sciences, at the School of Public Health.

The principles and techniques of **tissue culture** will be presented for medical research workers July 6-31 at the University of Colorado Medical School, by the Tissue Culture Association. This 26-day course at a fee of $100 will include laboratory work, seminars, lectures, with the enrollee performing as well as observing the procedures. Further information may be obtained from Dr. Mary S. Parshley, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York City 32.

MEDICAL NEWS

ARIZONA

Hospital Plans Neurological Wing.—A new four-story neurological wing costing more than one million dollars will be added to St. Joseph's Hospital, Phoenix, with construction starting in about a year. The addition is made possible by a gift from Charles A. Barrow and his family, of Litchfield Park, and his mother Mrs. Beatrice H. Barrow, of Franklin, Pa. Their donation of more than $500,000 is being matched with federal funds. The new wing will be known as the Barrow Neurological Institute, honoring the memory of the late William E. Barrow, father of Charles and husband of Beatrice Barrow. It will be devoted to diagnosis, treatment, research, and training in neurology and neurological surgery and will be headed by Dr. John R. Green, of Phoenix, chairman of neurology and neurological surgery at St. Joseph's. The Barrow Institute will have 50 beds at the outset plus surgery and clinical and research laboratories.

CALIFORNIA

Dr. Daniel Blain Named Director of Mental Health.—Dr. Daniel Blain, of Philadelphia, was named state director of mental hygiene, succeeding Dr. Marshall E. Porter, who will return to his former position as deputy director. A native of China and the son of missionary parents, Dr. Blain has been professor of clinical psychiatry at the University of Pennsylvania since 1958 and for 10 years before that was medical director of the American Psychiatric Association in Washington, D. C. The new mental hygiene chief is presently serving part-time as director of mental health work for the Western Inter-State Commission on Higher Education.

Society News.—At a meeting Jan. 20 of the Los Angeles Society of Allergy the following officers were elected for 1959: Dr. Ralph Bookman, president, Beverly Hills; Dr. Isadore Pitesky, vice-president, Long Beach; and Dr. Catherine G. Pearson, secretary-treasurer, Pasadena.——The officers for 1959 for the Metropolitan Dermatological Society of Los Angeles are: president, Dr. Eliot Wolk, Sherman Oaks; vice-president, Dr. Max Popper, Beverly Hills; and secretary-treasurer, Dr. Murray C. Zimmerman, 301 E. Hadley St., Whittier, Calif.

Plan New Research Center.—The Cedars of Lebanon Hospital announced plans for the construction of a new research center. The new facility will be a two-story and full basement building of steel and reinforced concrete. This expansion will enable the hospital to extend its research activity beyond the 100 scientific studies presently conducted there during the year, according to Dr. Leo G. Rigler, Cedars executive director. The chairman of the 11-million-dollar Cedars Medical Center Campaign, currently in progress, is Alfred Hart, hospital trustee and president of the City National Bank of Beverly Hills. Now under construction as another step in the Cedars Medical Center expansion program is the new Rehabilitation Center, totaling one million dollars and designed for treating arthritis, multiple sclerosis, heart disease, and crippling involvements.

CONNECTICUT

Fund to Honor Dr. Hamilton.—Dr. Alice Hamilton, of Hadlyme, a founder of the profession of occupational medicine, was honored on her 90th birthday Feb. 27 by the establishment of a fund bearing her name at the Harvard School of Public Health, Boston. Dr. Hamilton is assistant professor of industrial medicine, emerita, at Harvard. She served first the Harvard Medical School and then the School of Public Health from 1919 until her retirement in 1935. Dr. John C. Snyder, dean of the Harvard School of Public Health, said the Alice Hamilton Fund for Occupational Medicine was made possible by contributions from friends, admirers, former colleagues, and students of Dr. Hamilton. In 1910, when the State of Illinois started the first comprehensive survey of occupational disease, Dr. Hamilton became the survey's director. In 1919 she joined the faculty of medicine at Harvard as assistant professor of industrial medicine.

DISTRICT OF COLUMBIA

Dedicate Pre-Clinical Science Building.—The dedication exercises of the Pre-Clinical Medical Science Building at Howard University College of Medicine, Washington, were held Sept. 15. The dedication speaker was Mrs. Agnes E. Meyer, LL.D., who spoke on "A Plea for Scientific Humanism." The new building occupies the location of the original Medical School-Hospital built in 1869. On the ground floor is a lecture hall with a capacity of 250 persons, designed for use by outside groups for scientific meetings and other purposes. The

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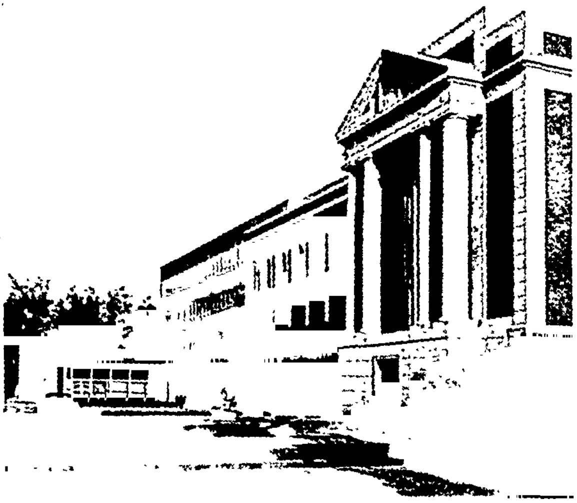
Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

department of anatomy has its office and gross anatomy sections on this floor. The departments of pathology and physiology are on the second floor and those of biochemistry, microbiology, and pharmacology are on the third floor. The new department of preventive medicine and public health and the audio-visual aids section are on the South West Wing of the second floor. There are two amphitheater-type classrooms with a two-floor depth. The fourth and fifth floors are designed for research and animal care, and the sixth floor includes a unit for health care and study of insects. The fourth floor laboratories provide facilities for handling radioactive isotopes, high-speed centrifugation, thermal control, x-ray, and tissue culture. The fifth floor has facilities and operating suites for surgical procedures. Mordecai W. Johnson, LL.D., president of Howard University, presided at the ceremonies.



The new Pre-Clinical Medical Science Building at Howard University, Washington, D. C.

HAWAII

Hospital Celebrates Fiftieth Anniversary.—The Kauikeolani Children's Hospital of Honolulu is celebrating the 50th anniversary of its founding with scientific and social programs on April 19-22 at the hospital and at Princess Kaiulani Hotel in Waikiki. Dr. Tague C. Chisholm, of the University of Minnesota Medical School, Minneapolis, and Dr. J. Roswell Gallagher, director, *Adolescent Clinic*, Children's Hospital, Boston, will participate in the scientific program which also includes rounds at the hospital and at Hale Mohalu, Hansen's Disease Hospital. These meetings are open to the members of the medical profession. For information write Dr. Teruo Yoshina, Chief of Staff, Kauikeolani Children's Hospital, 226 N. Kuakini St., P. O. Box 3799, Honolulu 17, Hawaii.

ILLINOIS

Poison Control Centers.—Dr. Roland R. Cross, director, Illinois State Department of Public Health, on Feb. 16 announced that in January, 130 cases of accidental poisoning were reported to the department by local poison control centers in downstate Illinois. Thirty-one hospitals in 23 downstate communities cooperate in the state accidental poisoning report program. Each hospital provides emergency treatment and 24-hour telephone service to help physicians identify ingredients of various poisonous substances and to make treatment recommendations. All of the cases reported during January in downstate Illinois occurred in children under six years of age. Figures reported for the year 1958 indicated that 85% of all accidental poisoning occurs in children under 4 and that almost half of these cases involve a medicinal tablet of some form. Hospitals desiring to participate may address inquiries to Dr. Cross.

Chicago

Research Hospital Receives Merit Award.—Argonne Cancer Research Hospital received the U. S. Atomic Energy Commission's million-hour Award of Merit for safety Feb. 12. Dr. Leon O. Jacobson, professor of medicine at the University of Chicago and director of the hospital, accepted the award. Argonne Hospital is operated for the AEC by the University of Chicago as part of the University Clinics. Built in 1953, it reportedly was the first hospital especially designed and equipped to use all known radiation sources in studies of the treatment of cancer. The AEC Merit Award cites the hospital's freedom from accidents for 1,018,769 man hours from Nov. 2, 1955, to Sept. 30, 1958. It means that during this period no one working in the hospital lost any time from work because of injuries received on his job. Argonne Hospital employs 200 persons.

Lectures on Surgical History.—Thomas S. Jones, M.S., emeritus professor of medical and dental illustrations, University of Illinois, will present the *seventh in a series of lectures on the history of surgery* and related sciences at the International Surgeons Hall of Fame, 1524 Lake Shore Drive, March 24, 8 p. m., on "Evolution of Medical Illustrations." The lecture is open to physicians, medical personnel, and students, and to the public. There is no admission charge, but accommodations are limited to 300. For reservations, telephone Miss Virginia Cavanagh, MIchigan 2-3555, or write to Dr. Ross T. McIntire, executive director, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10. Dr. Edward L. Compere, chairman, department of orthopedic surgery, Northwestern University Medical School, will present the eighth lecture in the series April 14 on "The History of Surgery of Bones and Joints."

KANSAS

Professorship in Human Reproduction.—A research professorship in human reproduction at the University of Kansas School of Medicine was announced in January by Dean W. Clarke Wescoe. Named to the post is Dr. Thomas H. Clewe, who came to Kansas from the department of anatomy, Yale University, New Haven, Conn. Dr. Clewe's academic appointment with the University of Kansas is assistant professor, and he is associated with the departments of anatomy and obstetrics and gynecology. The professorship and appointment of Dr. Clewe was made possible through gifts to the Kansas University Endowment Association by friends of the university. A laboratory has been set up at the medical school where Dr. Clewe will conduct his study of the physiology of reproduction and application of tissue-culture techniques to the study of tubal function and fertilization.

KENTUCKY

Meeting on Public Health in Louisville.—The 11th annual Kentucky Public Health Association meeting is to be held at the Sheraton Hotel, Louisville, March 31-April 2, featuring addresses by Dr. Berwyn F. Mattison, executive director, American Public Health Association, and Dr. Gaithel L. Simpson, Greenville. An afternoon of "curbstone consultations" in the various disciplines of public health and another afternoon of special interest groups on school health, mental health, maternal and child health, public health tax, chronic diseases, and radiological health, are planned. April 2 will be devoted to section meetings. The health officers' section has Dr. Fred E. Tosh, assistant medical director, Communicable Disease Center, Kansas City Field Station, U. S. Public Health Service, to speak on "The Problem of Histoplasmosis," and Mr. Paul Vaal, director, St. Luke Hospital, Poison Control Center, Ft. Thomas, is scheduled to present a talk on "Poison Control Centers in Kentucky." The nurses' section has Dr. Walter D. Jones, medical director, District No. 4, Tuberculosis Hospital, Ashland, to speak on treatment trends in tuberculosis. At the laboratory section Dr. Malcolm L. Barnes, Louisville, and Morris Scherago, Ph.D., will discuss "The Relationship of the Division of Public Health Laboratories to the Private and Public Laboratory," and Milford Hatch, Ph.D., Atlanta, Ga., will speak on "Fluorescein-tagged Antibody Techniques in Rapid Diagnostic Procedures."

MASSACHUSETTS

Tufts Medical Alumni Dinner Meeting.—The annual Tufts Medical Alumni dinner meeting will be held on Wednesday evening, April 8, 1959, at the Somerset Hotel, Boston. The guest speaker will be Mr. Robert F. Kennedy, chief counsel, Senate Select Committee on Improper Activities in the Labor or Management Field. Other speakers will be President Nils Y. Wessell, Tufts University, and Dr. Joseph M. Hayman, dean of Tufts College Medical School. The 25-year class, M'34, will hold their 25-year reunion beginning April 6 and ending with the dinner meeting April 8. For information write Dr. Harry Blotner, Secretary, Tufts Medical Alumni Association, 136 Harrison Ave., Boston 11.

MICHIGAN

Lectureship Honors Dr. Darling.—An annual lectureship honoring Dr. Milton A. Darling, Detroit obstetrician and gynecologist, was announced Feb. 25 by Wayne State University College of Medicine. Dr. Darling was specifically cited for his contribution to medical education through his development of the resident training program in obstetrics and gynecology at Grace Hospital. He is president-elect of the Michigan State Medical Society, a past-president of the Wayne County Medical Society, and a diplomate of the American Board of Obstetrics and Gynecology.

Report of Rabies.—Four animal rabies cases were reported in Michigan during the first five weeks of 1959, and the Michigan Department of Health has urged dog and cat owners to have their animals vaccinated against rabies. The four rabies cases have been in widely scattered parts of the state. The first case was a pet dog owned by a farm family near West Branch. The dog died of rabies early in January after fighting with a wild skunk which presumably was rabid. A few days later, a young calf owned by a farmer north of Ann Arbor died of rabies. Source of the disease is not known in this case. Late in January, a dog owned by a family residing on the outskirts of Manistique died of rabies. A young boy was exposed to the disease by the dog and is receiving anti-rabies treatment. On Feb. 2, a pet cat owned by a family at Hart died of rabies. One member of the family was bitten by the cat nine days before it died and is receiving treatment. Sources of the rabies in the Manistique and Hart cases also are unknown. The calf rabies case was confirmed by tests made at the Pasteur Institute at the University of Michigan, Ann Arbor, and the other cases by tests at the Michigan Department of Health laboratories in Lansing. Last year Michigan had 38 animal cases and no human cases—there had not been a human case since 1948. The 38 cases in 1958 included 11 in the Upper Peninsula; 1958 was the first year since 1940 that rabies was reported north of the Straits.

MISSOURI

Annual Meeting in Kansas City.—The Missouri State Medical Association will hold its 101st annual session at the Muehlebach Hotel, Kansas City, April 5-8. Four panel discussions are planned and the following papers will be presented by out-of-state speakers:

Working Together for an Improved Missouri Mental Health Program, Dr. Addison M. Duval, Washington, D. C.
The Increasing Menace of Carcinoma of the Lung, Dr. Alton Ochsner, New Orleans.
Esophageal Hiatal Hernia, Dr. James H. Growdon, Little Rock, Ark.
Abnormal Uterine Bleeding, Dr. Roy G. Holly, Omaha.
Pancreatitis, Dr. Eric E. Wollaeger, Rochester, Minn.
Recent Advances in Roentgenology of the Biliary System, Dr. Lester W. Paul, Madison, Wis.
Present Day Concepts in the Treatment of Occlusive Cerebral Vascular Disease, Dr. Clark H. Millikan, Rochester, Minn.

Motion pictures, instruction courses, and exhibits are planned, and the annual banquet will be held April 7, 7:30 p.m., with Rev. Carl S. Winters, Oak Park, Ill., as speaker. Dr. Ferdinand C. Helwig, of Kansas City, will moderate a clinical pathologic conference the afternoon of April 6.

NEVADA

Cancer Seminar in Reno.—The American Cancer Society, Nevada Division, Inc., will present its annual Cancer Seminar March 25-26 at the Riverside Hotel, Reno. Two medical motion picture sessions on "Head and Neck Cancer, Tumors of Bone," and on "Moles and Melanomas, Tumors of Childhood" are planned. Four panel discussions have been arranged, and the following speakers and panelists are scheduled:

Drs. Weldon Bullock and Maurice Galante, Los Angeles; John W. Cline and Glenn Sheline, San Francisco; Edward C. Hammond, Ph.D. director, statistical research, American Cancer Society, Inc., John F. W. King, and Carnelius P. Rhoads, New York City; Peter A. Linstrom and Max W. Wintrobe, Salt Lake City; Kenneth C. Sawyer, Denver; and Michael B. Shimkin, Bethesda, Md.

The Seminar is certified for category 1 credit by the American Academy of General Practice. For information write Dr. Fred M. Anderson, 275 Hill St., Reno, Nev., Chairman, Seminar Committee.

NEW YORK

New York City

Dr. Lillehei to Lecture.—The third Bernard Sutro Oppenheimer Lecture will be given in Hosack Hall of The New York Academy of Medicine, 2 E. 103 St., April 2, 8:30 p. m. The lecturer will be Dr. C. Walton Lillehei, professor of surgery, University of Minnesota Medical School, Minneapolis. Dr. Lillehei's subject will be "Open Heart Surgery for Acquired and Congenital Heart Disease."

Dr. Kleiner Receives Award.—Israel S. Kleiner, Ph.D., director, department of biochemistry, New York Medical College, Flower and Fifth Avenue Hospitals, was awarded the third annual Van Slyke award of the New York Section, American Association of Clinical Chemists "in recognition of his pioneering contributions as a research investigator and as an educator." Dr. Kleiner lectured on "Hypoglycemic Agents—Past and Present."

Personal.—Dr. John J. Untereker, clinical instructor in physical medicine and rehabilitation at New York University-Bellevue Medical Center, was named director of the medical service at the Institute for the Crippled and Disabled, rehabilitation center at 23rd Street and First Avenue.—Dr. Nadene Coyne was appointed coordinator of training for physicians in the department of physical medicine and rehabilitation of New York University-Bellevue Medical Center and director of the Respirator Center at Goldwater Memorial Hospital.

Expand Rehabilitation Program.—The Institute for the Crippled and Disabled announced a major expansion of its education and training services for students and professional people pursuing careers in the rehabilitation of handicapped persons. To head its expanded program, the institute has named Isabel Pick Robinault, Ph.D., as director of professional education and training. At the College of Physicians and Surgeons, Columbia University, she is supervisor of postgraduate cerebral palsy courses and an instructor in occupational therapy. According to Dr. Robinault, the expanded program will offer opportunities in professional rehabilitation specialties to persons engaged in undergraduate as well as graduate study. Technical training in nonprofessional subjects will be provided. Among the joint rehabilitation teaching activities of New York University and the Institute for the Crippled and Disabled is vocational rehabilitation counselor training for graduate students. Teaching activities to be continued include courses of 10 months duration for makers and fitters of artificial limbs and braces, clinical affiliations for occupational and physical therapy undergraduates and for graduate nurses, psychologists, and rehabilitation counselors, a three-week course on the teamwork concepts of rehabilitation center operation, and six-week training programs in the conduct of vocational evaluation programs for the disabled. The faculties will be drawn from the staff of the institute and the faculty of N. Y. U. Wherever feasible, a course will be offered in collaboration with New York University and other participating institutions and college credits will be given.

OKLAHOMA

New Low in Maternal Deaths.—A new low of 3.7 maternal deaths per 10,000 live births, the lowest figure ever recorded in Oklahoma, is contained in a recent report by the division of vital statistics at the Oklahoma State Department of Health. Sepsis, toxemia, and hemorrhage are the major causes of maternal mortality now as they were 30 years ago, or even 10 years ago, according to Dr. John W. Shackleford, director of the division of maternal and child health.

OREGON

Annual Alumni Meeting.—The 44th annual meeting of the University of Oregon Medical School Alumni Association will be held April 8-10 in the school's library auditorium, Portland, according to Dr. John F. Larsell, president of the association. Registration will be 9-10 a. m. on the opening day. The group's scientific session will be presented in conjunction with the Sommer Memorial Lectures. Category 2 postgraduate credit will be allowed for members of the American Academy of General Practice attending the meeting. Evening social events will include fraternity reunions on April 7; the invitational Sommer Memorial Lecture banquet, April 8; the Alumni Association banquet, April 9 at Piluso's restaurant; and class reunions, April 10. Classes planning reunions include '34, '39, '49, and '54. The alumni will elect new officers and hear committee reports at the annual business meeting scheduled for the morning of April 9.

PENNSYLVANIA

Program for Training of Geneticists.—The department of biostatistics in the University of Pittsburgh Graduate School of Public Health will start training human geneticists next September. The purpose of this program will be to train research scientists who will study hereditary aspects of various diseases, particularly those relating to public health problems. Ching Chun Li, Ph.D., associate professor of biostatistics, will direct the new program. Dr. Li, who was head of the department of agronomy at National Peking (China) University, has been on the faculty of The Pitt Graduate School of Public Health since 1951. He has specialized in population genetics and is currently president-elect of the Society of Human Genetics. The program has been designed for advanced students who are trained in biology and have received at least a master's degree. The course of study will be tailored to the background and research interest of each student.

TEXAS

Annual Clinical Conference in Dallas.—The 28th annual spring clinical conference of the Dallas Southern Clinical Society will be held March 23-25 at the Statler Hilton Hotel, Dallas. Postgraduate lectures, round-table luncheons, panel discussions, and exhibits are planned. The following are listed as guest speakers:

Drs. Leo H. Bartemeier, Baltimore; Elmer Belt, Howard P. House, and J. Vernon Luck, Los Angeles; Edward P. Cawley, Charlottesville, Va.; Robert J. Coffey and Frank D. Costenbader, Washington, D. C.; Jerome W. Conn, Ann Arbor, Mich.; Charles Eckert, Albany, N. Y.; Philip J
Hodes, Irving H. Leopold, and William A. Sodeman, Phila
delphia; Charles A. Janeway and Frank D. Lathrop, Bos
ton; John W. Kirklin, Rochester, Minn.; Frank R. Lock
Winston-Salem, N. C.; Samuel B. Nadler, New Orleans
and Ernest Winslow, San Francisco

For information write the Dallas Southern Clin
ical Society, 433 Medical Arts Building, Dallas
Texas.

VERMONT

General Practice Meeting in Burlington.—A regul
meeting of the Vermont Chapter, American Aca
emy of General Practice, will be held March 26
the DeGoesbriand Memorial Hospital Auditoriu
beginning at 9:30 a.m. Dr. John C. Twitchell, Bu
lington, has arranged the following papers by Bu
lington participants:

New Approaches to Speech and Hearing Rehabilitation, I
troduction: Dr. Robert P. Smith.
Management of Hearing Loss; Medical-Surgical Aspec
Dr. Rufus C. Morrow.
Management of Speech Disturbances, (1) Neurological
pects: Dr. Herbert L. Martin; (2) Rehabilitation Aspec
Frank J. Falck, Ph.D.
Treatment of Coronary Insufficiency, 'Dr. Ellsworth L. Ar
don.
Modern Concepts in Therapy of Tuberculosis, Dr. Sinclair Allen.
Oral Treatment of Diabetes, Dr. George W. Welsh, III.
The Neurological Examination, Dr. George A. Schumach

VIRGINIA

Annual Lecture.—The Alpha Mu chapter of the P
Delta Epsilon Fraternity will hold its annual le
tureship series March 21 at 10:30 a. m. in the B
Johnston Auditorium of the Medical College
Virginia, Richmond. The guest speaker will be I
Cushman D. Haagensen, professor of surgery, C
lumbia University College of Physicians and S
geons, New York City. His subject is "Current Th
apy of Carcinoma of the Breast."

GENERAL

Glaucoma Identification Card.—A glaucoma iden
fication card for nationwide distribution was
nounced by The National Medical Foundation
Eye Care. The card, similar in purpose to
diabetes identification card, will alert examini
physicians that the patient has glaucoma and
using drugs. The names of the patient and of
ophthalmologist who prescribed the drugs appe
on the card, together with the prescription. T
glaucoma card also carries the spectacle prescr
tion of the patient. The cards were printed as
public service by Abbott Laboratories, and are
ing initially distributed to physicians by the labo
tories. Packets of the cards may be obtained
writing to the foundation office, 250 W. 57th
New York 19, or directly to Professional Servic
Abbott Laboratories, North Chicago, Ill. Educati
of the general public to the threat of glaucoma a

other eye diseases, with emphasis on the importance of regular medical eye care, is a basic purpose of The National Medical Foundation for Eye Care.

National Meeting of Chemists in Boston.—The 135th national meeting of the American Chemical Society will be held in Boston April 5-10. Chemists and chemical engineers from the United States and foreign countries will hold technical sessions in 10 of Boston's major hotels and auditoriums throughout the week, with the society's Northeastern Section as host. Prof. John C. Bailar Jr., of the University of Illinois, president of the society, will preside at a general assembly in John Hancock Hall April 6. Nobel Prize-winning chemist, Vincent du Vigneaud, head, department of biochemistry, Cornell Medical College, New York City; Prof. Robert B. Woodward, of Harvard, Boston; and Lewis H. Sarett, Ph.D., of Merck, Sharpe & Dohme Research Laboratories, Rahway, N. J., will attend. Progress in cancer research, chemical investigation in the fields of vitamins, proteins, and hormones and the development of a new class of antidepressant compounds will be discussed in sessions of the divisions of medicinal and biological chemistry. A report also will be made on recent research on the physiological effects of tobacco smoke. The American Chemical Society has more than 86,000 members and has 155 local sections serving 48 states, the District of Columbia, Puerto Rico, and Hawaii.

Select Orthopedic Surgeons as Exchange Fellows. Four American orthopedic surgeons selected as exchange fellows for a 7-week visit to England this spring are Dr. James S. Miles, University of Colorado Medical Center; Dr. Sherman S. Coleman, of the University of Utah School of Medicine; Dr. John P. Adams, Washington, D. C.; and Dr. Andrew H. Crenshaw, of Memphis, Tenn. They were advised of their selection by the American Orthopedic Association, which designates the visiting group every other year. The British Orthopedic Association makes the selections in the even years, and sent five physicians to the U. S. in 1958. The four surgeons will sail on the Queen Mary in April. During the stay in England the group will visit orthopedic centers and hospitals, will attend scientific meetings and conferences, and will be guests at social functions. Their expenses will be paid by the American Orthopedic Association. The U. S. quartet will have an audience with Queen Elizabeth, and will attend the annual meeting of the British association in May. They will return to the United States on the liner Queen Elizabeth in time for the meeting of the American Orthopedic Association at Lake Placid, N. Y., June 16-18. Physicians selected for participation in the exchange fellow program are under 40 years of age and are chosen for their "outstanding records and their professional interest in either private or academic medicine."

Award for Research in Norway.—The American-Scandinavian Foundation, which each year offers a number of awards for study in Scandinavia as part of its program to increase understanding between the United States and the Scandinavian countries, has announced the availability of one Clifford N. Carver Fellowship of $900 in Norwegian currency for medical research in Norway. Applicants must be American Citizens who have completed their college education. Ordinarily they should be under 40 years of age. No knowledge of Norwegian is required. Applicants will be judged on their plan of study and their ability to carry it out as indicated in the completed application. It is important that the plan of study be fully explained: it should be stated where the work will be done, the reasons for wishing to undertake or continue studies in the particular field, and the long-range professional objectives. The grants may be used in any way the grantee sees fit to aid him in his study. Normally they are paid in four installments. It is expected that the award winner will spend an academic year abroad. Applicants should plan to begin their study not later than Jan. 1. While an applicant may also apply for grants through other organizations, winners of ASF awards should not accept any other award without first consulting the foundation. Applications close April 1. For information and application, write the American-Scandinavian Foundation, 127 E. 73d St., New York 21.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing application is June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Examination.* Phoenix, Apr. 15-17. *Reciprocity and Endorsement.* Phoenix, April 18. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

Delaware: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

Florida:* *Examination.* Miami Beach, June 21-23. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, June 10-11. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Idaho: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Examination.* Chicago, April 6-9. *Reciprocity.* Chicago, April 10. Supt. of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

Indiana: *Examination.* Indianapolis, June 17-19. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Iowa:* *Examination.* Iowa City, June 15-17. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines 19.

Kansas:* *Examination and Endorsement.* Kansas City, June. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination.* Louisville, June 8-10. Sec., Dr. Russell E. Teague, 620 South Third St., Louisville 2.

Maine: *Examination and Reciprocity.* Portland, March 10-12. Sec., Dr. Stephen A. Cobb, Sanford.

Maryland: *Examination.* Baltimore, June 23-26. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Michigan:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minneapolis:* *Examination.* Minneapolis, April 21-23. *Reciprocity.* Minneapolis, April 23. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Mississippi: *Examination and Reciprocity.* Jackson, June 22-24. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Missouri: *Reciprocity.* Kansas City, April 6. *Examination.* St. Louis, May 29-30. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

Montana: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

Nevada:* *Examination and Reciprocity.* Reno, March 3. Sec., Dr. G. H. Ross, 112 North Curry St., Carson City.

New Jersey: *Examination.* Trenton, June 16-19. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

New Mexico:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* New York, Rochester, Syracuse, Buffalo and Albany, June 23-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

North Carolina: *Examination.* June 15-18. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Ohio: *Endorsement.* Columbus, April 7. *Examination.* Columbus, June 18-20. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

Oklahoma:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon:* *Written.* Portland, Apr. 17-19. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination and Endorsement.* Philadelphia and Pittsburgh, July 1-3. Sec., Mrs. Margaret G. Steiner, Box 911 Harrisburg.

Rhode Island:* *Endorsement.* Providence, March 26. *Examination.* Providence, April 2-3. Administrator of Professional Education, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Reciprocity.* Columbia, May 12; *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Tennessee:* *Examination.* Memphis, March 25-26. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

Texas:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination and Reciprocity.* Salt Lake City, July 810, Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Virginia: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

Washington:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Reciprocity and Endorsement.* Charleston, April 13. *Examination.* Charleston, June. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Madison, April 17 and Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, June 1. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arizona: *Examination.* Tucson, March 17. Sec., Mr. Herman E. Bateman, University of Arizona, Tucson.

Arkansas: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

Colorado: *Examination.* Denver, May 6-7. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, June 6. Exec. Asst. Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, May 18-19. Address: Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.

Florida: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Iowa: *Examination.* Des Moines, April 14. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

Kansas: *Examination.* Kansas City, June 2-3. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, May 8-9. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, April 7-8. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

Nebraska: *Examination.* Omaha, May 5-6. Director, Mr. R. K. Kirkman, Bureau of Examining Boards, 1009 State Capitol Bldg., Lincoln.

New Mexico: *Examination.* Santa Fe, April 19. Sec., Mrs. Marguerite Cantrell, P. O. Box 1522, Santa Fe.

Oklahoma: *Examination.* Oklahoma City, Mar. 27-28. Exec. Sec., Mrs. L. Haidek, 813 Braniff Bldg., Oklahoma City.

South Dakota: *Examination.* Vermillion, June 5-6. Sec., Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Tennessee: *Examination.* Memphis, Mar. 25-26. Sec., Dr. O. W. Hyman, 62 South Dunlap St., Memphis 3.

Texas: *Examination.* Austin, Galveston, Houston, Apr. 17-18. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Washington: *Examination.* Seattle, July 8-9. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin: *Examination.* Madison, April 4. Final date for filing application is March 27. Milwaukee, June 6. Final date for final application is May 29. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

Neuropsychiatric Meeting.—The Ninth Annual Institute in Psychiatry and Neurology, sponsored by the VA Hospital, Lyons, N. J., and the New Jersey Neuropsychiatric Association, will be held Wednesday, April 1, at the VA Hospital, Lyons, N. J. The registration fee is $1. Military personnel and full-time veterans administration personnel may register without charge. The meeting will be held in building 5 and will start at 10 a. m. The program for the morning session will be as follows:

Relation of Epinephrine and Norepinephrine to Psychophysiologic Disease by William M. Manger, M.D., and Eric B. Schwarz, M.D.

Research in Social Psychiatry: Goals and Guidelines by Leo Srole, Ph.D.

Ego Breakdown in Schizophrenia and Its Implication for Casework Treatment by Esther S. Marcus, M.S.

Treatment of Hemiplegia by John Untereker, M.D.

The program for the afternoon session under the chairmanship of Ralph E. Snyder, M.D., will be:

Abnormality of Cerebral Transmission—A Neurophysiological Approach to Cerebral Disturbance by Amadeo Marrazzi, M.D.

The Current Status of Tranquilizers by Frank Ayd Jr., M.D.

Depressions—Recognition and Treatment by Leo Alexander, M.D.

The after-dinner speaker, Allan B. Monro, M.D., superintendent, Long Grove Hospital, Epsom Surrey, England, has for his subject "Comparative Aspects of British and American Psychiatry."

Dr. Barnwell Honored.—Dr. John B. Barnwell of the Veterans Administration was selected as one of the 10 top career men in the federal government for 1958-1959 by the National Civil Service League. The honor carries with it one of the league's annual Career Service awards. Dr. Barnwell, who heads medical research and education for the VA in Washington, D. C., was cited for his part in organization of the VA-Armed Forces cooperative study of chemotherapy of tuberculosis.

PUBLIC HEALTH SERVICE

Manual on Staphylococcic Diseases.—The Communicable Disease Center, Atlanta, Ga., has developed a 289-page training reference entitled, "Selected Materials on the Environmental Aspects of Staphylococcal Diseases." This volume, compiled by the Environmental Health Training Section, consists of 30 reprints together with appendices of additional readings, available training aids, outline of the hospital environment, and sources of further assistance. The selected articles contain information on hospital design; water and liquid waste disposal; solid waste storage, collection, and disposal; air hygiene; laundry and linen service; housekeeping; disinfection and sterilization; and the hospital environment in general. Copies of the manual are available from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C., at a cost of $1.50 per copy.

CIVIL SERVICE COMMISSION

Openings for Physicians.—About 200 medical officers will be needed by the federal government this year for professional assignment in all of the specialties. Experience requirements range from doctors who have just completed their internship to those who have had highly responsible professional experience. The positions are located throughout the United States and in foreign countries. Starting salaries range from $7,510 to $12,770 a year. The major employers of medical officers in the federal government are the Army, Navy, and Air Force installations (civilian service); the Public Health Service; Indian Service Hospitals; the Food and Drug Administration; St. Elizabeths Hospital in the District of Columbia; and the Children's Bureau.

Federal medical officers have an opportunity to do challenging research work in helping to maintain national health and to search for the causes of human diseases. They also care for patients in hospitals, clinics, military establishments, and other government organizations. The greatest need in these establishments has been in the fields of general medicine and surgery, nutrition, public health, tuberculosis, venereal disease, roentgenology, pathology, radiology, physical medicine and rehabilitation, and psychiatry. Medical officers serve as consultants in the administration of state medical programs, conduct programs and supervise medical personnel in industrial establishments which are under the direction of federal departments, or conduct health programs in a federal agency. They also make medical decisions which affect the enforcement of federal laws and claims for compensation on the basis of physical and mental disability, and they perform many other types of administrative work. Doctors who desire further information regarding these positions should obtain a copy of Announcement 178 at a post office or from the U. S. Civil Service Commission, Washington 25, D. C. Applications will be accepted until further notice.

DEATHS

Auslander, Morris, New York City; University and Bellevue Hospital Medical College, New York City, 1908; veteran of World War I; since 1942 served on the local Selective Service Board; formerly on the staff of the Lutheran Hospital; died Jan. 5, aged 71.

Barlow, Edward Callistus Ⓜ Georgetown, Ky.; Pulte Medical College, Homeopathic, Cincinnati, 1901; veteran of World War I; died in the John Graves Ford Memorial Hospital Nov. 17, aged 82.

Barnebee, James William Ⓜ Kalamazoo, Mich.; Rush Medical College, Chicago, 1901; formerly practiced in Mendon, where he was health officer for many years; associated with the Bronson and Borgess hospitals; served as examining physician for the local Selective Service Board; died in the Bronson Hospital Dec. 19, aged 80.

Beasley, Thomas J. Ⓜ Indianapolis; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; veteran of the Spanish-American War; served on the staffs of the Methodist, Community, and Indianapolis General hospitals; died Dec. 30, aged 78.

Benkendorf, Richard Clark Ⓜ Bushnell, Ill.; Chicago Medical School, 1936; member of the American College of Chest Physicians and the American Trudeau Society; veteran of World War II; member of the city health department; on the staff of St. Francis Hospital in Macomb, where he died Jan. 8, aged 50.

Blau, Arthur Isidor, New York City; University and Bellevue Hospital Medical College, New York City, 1913; a senior public health physician with the city department of health; served as health officer in Harlem, in the Red Hook–Gowanus district of Brooklyn and in Jamaica, Queens, and also as health officer of the Borough of Queens; in 1947-1948 directed the Bureau of Health Education; past-president of the Greater New York Public Health Officers' Association; died in the Memorial Hospital Jan. 8, aged 67.

Brake, C. Bernard, Dearborn, Mich.; Detroit College of Medicine and Surgery, 1921; died Dec. 10, aged 68.

Brooks, Everett Hayden Ⓜ Bloomington, Wis.; the Hahnemann Medical College and Hospital, Chicago, 1897; for many years practiced in Appleton; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; died Dec. 17, aged 86.

Brown, James Erroll Ⓜ Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1904; an associate member of the American Medical Association; died Dec. 16, aged 79.

Brown, James Steven Sr., Hendersonville, N. C.; Northwestern University Medical School, Chicago, 1893; associated with Margaret R. Pardee Memorial Hospital, where he died Dec. 26, aged 92.

Burthe, Joseph Leopold, New Orleans; Medical Department of Tulane University of Louisiana, New Orleans, 1897; died in the Ochsner Foundation Hospital Dec. 30, aged 83.

Bushman, Louis Bernard Ⓜ Omaha, Neb.; John A. Creighton Medical College, Omaha, 1903; for many years on the faculty of his alma mater; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; associated with St. Catherine's Hospital, Douglas County Hospital, and Creighton Memorial St. Joseph's Hospital, where he died Dec. 30, aged 81.

Carman, William L., Irwin, Pa.; Kentucky School of Medicine, Louisville, 1905; veteran of World War I; died in the Veterans Administration Hospital, Pittsburgh, Dec. 3, aged 81.

Chiles, William Wallace, Chesterfield, S. C.; University of Arkansas School of Medicine, Little Rock, 1927; veteran of World War I; died Dec. 16, aged 65.

Chung, Margaret Jessie, San Francisco; College of Physicians and Surgeons, medical department of the University of Southern California, Los Angeles, 1916; for a short time psychiatric criminologist for Illinois; at one time associated with Kankakee (Ill.) State Hospital; died Jan. 5, aged 69.

Crawford, Frank Wallis Ⓜ Holbrook, Mass.; Tufts College Medical School, Boston, 1909; veteran of World War I; past-president of the Norfolk South District Medical Association; past-president and charter member of the Randolph Rotary Club; associated with the Goddard Memorial Hospital in Brockton and South Shore Hospital in Weymouth; died Dec. 30, aged 76.

Ⓜ Indicates Member of the American Medical Association.

Critchfield, Charles Louis, Waverly, Ohio; Ohio State University College of Medicine, Columbus, 1938; formerly associated with the Orient (Ohio) State School; died Dec. 30, aged 46.

Crocker, Samuel H., Stantonsburg, N. C.; Kentucky School of Medicine, Louisville, 1894; served as mayor of Stantonsburg and as chairman of the school board; instrumental in organizing the Planters Bank and served as its first president; for many years a director of the Federal Land Bank of Columbia, S. C.; died Dec. 13, aged 91.

Croom, Gabe Holmes Ⓜ Asheville, N. C.; North Carolina Medical College, Charlotte, 1909; served overseas during World War I; died Dec. 26, aged 74.

Davis, John Joseph Ⓜ Brooklyn; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1894; died Dec. 10, aged 85.

Deich, Jacob Frank Ⓜ Boston; Tufts College Medical School, Boston, 1927; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the International College of Surgeons and the American College of Surgeons; served on the faculty of his alma mater; on the staffs of the Boston City and Beth Israel hospitals; died Dec. 28, aged 54.

DeLancy, Oscar Minton, Clovis, Calif.; Washington University School of Medicine, St. Louis, 1922; died Dec. 18, aged 63.

Dickson, Harry Ellis, Marietta, Ohio; Ohio State University College of Medicine, Columbus, 1914; died Dec. 27, aged 70.

Dieffenbach, Richard Hagen Ⓜ Newark, N. J.; born in 1883; Columbia University College of Physicians and Surgeons, New York City, 1904; member of the founders group of the American Board of Surgery; specialist certified by the American Board of Thoracic Surgery; member of the American Association for Thoracic Surgery and New York Thoracic Society; fellow of the American College of Surgeons; past-president of the Anatomical and Pathological Society of New Jersey; associated with Clara Maass Memorial Hospital, where he was for many years president of the staff, and the Essex County Hospital in Belleville, Alexian Brothers Hospital in Elizabeth, St. Mary's Hospital in Orange, Columbus Hospital, Martland Medical Center, St. Barnabas Medical Center, St. Michael's Hospital, St. James Hospital, Newark Eye and Ear Infirmary, and Presbyterian Hospital; member of the board of directors of the Bank of Commerce; died Jan. 2, aged 75.

Dredge, Homer Percy Ⓜ Sandstone, Minn.; Rush Medical College, Chicago, 1896; for many years health officer; served as president of the Pine County School Board; for many years member of the school board; at one time practiced in Belview and served as coroner of Redwood County; in 1955 was selected as the first member of the Sandstone Hall of Fame; died in the Asbury Hospital, Minneapolis, Nov. 27, aged 88.

Epeneter, Franz Joseph, Portland, Ore.; State University of Iowa College of Medicine, Iowa City, 1911; died in the Physicians and Surgeons Hospital Dec. 29, aged 69.

Fitzgerald, Don Felipe Ⓜ Wayzata, Minn.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; died at Lake Minnetonka Dec. 8, aged 91.

Fonvielle, William Bassette Ⓜ Rockford, Ill.; Howard University College of Medicine, Washington, D. C., 1928; member of the American Academy of General Practice; veteran of World War II; on the staff of St. Anthony Hospital; died Dec. 31, aged 59.

Fowler, Russell Story, Brooklyn; Columbia University College of Physicians and Surgeons, New York City, 1895; past-president of the Medical Society of the County of Kings, the Brooklyn Surgical Society, and the Clinical Society of Wyckoff Heights Hospital; specialist certified by the American Board of Surgery; founder, life member, and past-governor of the American College of Surgeons; honorary director emeritus of surgery at the Wyckoff Heights Hospital, where for many years he was chief surgeon; consultant, Methodist, Maimonides, and Bay Ridge hospitals; author of many books on surgery; died Jan. 5, aged 84.

Fraser, Noah Edward, Conway, Ark.; Memphis (Tenn.) Hospital Medical College, 1908; past-president of the Faulkner County Medical Society; on the staff of the Conway Memorial Hospital, where he died Dec. 21, aged 78.

Frazier, Harry Orwin Ⓜ Salt Lake City, Utah; University of Nebraska College of Medicine, Omaha, 1936; past-president and secretary of the Intermountain Ophthalmological Society and the Pan American Association of Ophthalmology; veteran of World War II; on the staff of the Latter-Day Saints Hospital; died Dec. 31, aged 52.

Geoghegan, Thomas Whitney, St. Paul, Minn.; University of Buffalo School of Medicine, 1925; medical director of the St. Paul Red Cross Program; served during World War II and was decorated for his services in the South Pacific; died Jan. 10, aged 57.

Gold, Bertha Benjamin, Jersey City, N. J.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1897; vice-president and board member of the Hudson County Hebrew Home for Orphans and Aged; died Jan. 9, aged 84.

Grace, Joseph B., Bismarck, N. D.; John A. Creighton Medical College, Omaha, 1912; died Dec. 21, aged 77.

Groebner, Otto Andrew Ⓜ Sioux Falls, S. D.; University of Minnesota Medical School, Minneapolis, 1917; served overseas during World War I; on the staffs of the Sioux Valley and McKennan hospitals; died Dec. 21, aged 65.

Hamilton, Burke Coonley, New York City; Syracuse University College of Medicine, 1906; veteran of World War I; served with Red Cross commission to Balkan States; died in St. Vincent's Hospital Dec. 21, aged 77.

Harding, James Sylvester, Baltimore; George Washington University School of Medicine, Washington, D. C., 1924; on the staffs of Bon Secour Hospital and St. Joseph's Hospital, where he died Dec. 20, aged 60.

Hartmann, Richard Anthony Ⓜ Effingham, Ill.; Stritch School of Medicine of Loyola University, Chicago, 1951; member of the American Academy of General Practice; past-president of the Effingham County Medical Society; on the staff of St. Anthony Hospital; died in Hollywood, Calif., Jan. 1, aged 35.

Hollingshead, Lyman Benajah, Springfield, Ill.; Medico-Chirurgical College of Philadelphia, 1906; veteran of World War I; formerly practiced in Pemberton, N. J., where he served as mayor; died Nov. 18, aged 82.

Holmes, Hal Buck, Conway, S. C.; Medical College of South Carolina, Charleston, 1926; veteran of World War I; on the staff of the Conway Hospital; died in Myrtle Beach Dec. 27, aged 62.

Howard, Marion Edith, Cali, Colombia, South America; Johns Hopkins University School of Medicine, Baltimore, 1931; served as assistant physician at the Johns Hopkins Hospital and Dispensary; formerly an intern and resident at the New Haven (Conn.) Hospital; for many years on the faculty of Yale University School of Medicine in New Haven, Conn., where she was associate clinical professor of medicine, and associate physician, department of university health; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; died Jan. 5, aged 59.

Huff, Bolivar, Camp Verde, Ariz.; University Medical College of Kansas City, Mo., 1900; formerly associated with the Indian Service; died in the Good Samaritan Hospital, Phoenix, Dec. 5, aged 89.

Hurley, George Ira, Eugene, Ore.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; fellow of the American College of Surgeons; served overseas during World War I; on the staff of the Sacred Heart Hospital; died Dec. 31, aged 81.

Hurst, Julius Harold, Lubec, Maine; Yale University School of Medicine, New Haven, 1904; Columbian University Medical Department, Washington, D. C., 1903; veteran of World War I; fellow of the American Association for the Advancement of Science; formerly associated with the U. S. Public Health Service and Veterans Administration; died in the New England Baptist Hospital, Boston, Dec. 10, aged 85.

Johnston, Henry Vernon Ⓜ Pungo, Va.; Columbian University Medical Department, Washington, D. C., 1907; died in the Walter Reed Army Hospital, Washington, D. C., Dec. 21, aged 75.

Kobes, Herbert Richard Ⓜ Springfield, Ill.; Harvard Medical School, Boston, 1930; clinical associate professor of pediatrics, University of Illinois College of Medicine; specialist certified by the American Board of Pediatrics and the American Board of Preventive Medicine; member of the American Academy of Pediatrics and the American Public Health Association; director of the University of Illinois Division of Services for Crippled Children in Springfield since 1945; director of the Center for Handicapped Children at Research and Educational Hospitals; died Jan. 10, aged 54.

Koory, Shickrey B., Woodland Hills, Calif.; Creighton University School of Medicine, Omaha, 1907; at one time on the faculty of his alma mater; died in Van Nuys Nov. 6, aged 74.

Laguardia, Attilio, New York City; born Sept. 23, 1903; Columbia University College of Physicians and Surgeons, New York City, 1927; specialist certified by the American Board of Psychiatry; member of the American Psychiatric Association; formerly on the faculty of the Ohio State University College of Medicine in Columbus; assistant commissioner of mental hygiene for the state of Ohio from 1945 to 1947; from 1947 to 1949 chief of mental hygiene for the Veterans Administration office in Columbus, Ohio; for many years associated with the Rockland State Hospital in Orangeburg, N. Y.; on the staff of the Hillside Hospital; died in the University Hospital Jan. 5, aged 55.

Molliver, Henry Ⓜ Chelsea, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1933; on the staff of the Chelsea Memorial Hospital; member of the American Academy of General Practice; died in the Beth Israel Hospital Dec. 23, aged 54.

Perry, Julia Wygant, Forest Hills Gardens, N. Y.; Woman's Medical College of Pennsylvania, Philadelphia, 1891; died Dec. 17, aged 94.

Preiser, Samuel Aaron, New York City; Long Island College Hospital, Brooklyn, 1910; associated with Mount Sinai, Beth Israel, and Montefiore hospitals; died in the Bellevue Hospital Dec. 4, aged 74.

Reeves, John Herbert Ⓜ Chicago, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1896; veteran of World War I; died Jan. 14, aged 84.

Simmons, Albert Vander Veer Ⓜ Maplewood, N. J.; University and Bellevue Hospital Medical College, New York City, 1907; for many years on the staff of the Orange (N. J.) Memorial Hospital; died in Ballston Spa Jan. 4, aged 74.

Smith, Gilbert Elden Ⓜ Spartanburg, S. C.; University of Illinois College of Medicine, Chicago, 1934; specialist certified by the American Board of Radiology; on the staff of the Spartanburg General Hospital; died Dec. 3, aged 50.

Standish, James Herbert Ⓜ Hartford, Conn.; University of the City of New York Medical Department, New York City, 1895; on the courtesy staffs of Hartford and St. Francis hospitals; died Dec. 22, aged 88.

Sterrett, William Preston Ⓜ Humansville, Mo.; Ensworth Medical College, St. Joseph, 1900; past-president of the Wyandotte County (Kan.) Medical Society; served on the faculty of the University of Kansas School of Medicine in Kansas City, Kan., where he practiced for many years and where he was on the staff of the Bethany Hospital, where he died Dec. 19, aged 99.

Strack, Gustave Ⓜ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1903; died in the Brooklyn Hospital Nov. 12, aged 83.

Swartz, George Krumrine Ⓜ Fort Myers, Fla.; born in Tusseyville, Pa., April 23, 1897; University of Pennsylvania School of Medicine in Philadelphia, 1924; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War I; formerly associated with the U. S. Public Health Service Reserve; at one time on the faculty of his alma mater and Baylor University College of Medicine in Houston, Texas; at various times affiliated with the Veterans Administration Hospital in Coatesville, Pa., on the staff of the Norristown (Pa.) State Hospital, Battle Creek (Mich.) Sanitarium, and the Missouri Baptist Hospital in St. Louis; died in the Lee Memorial Hospital Dec. 20, aged 61.

Thomas, Joseph Edward Ⓜ Plant City, Fla.; born in Studa, Pa., Oct. 30, 1921; Georgetown University School of Medicine, Washington, D. C., 1948; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; interned at St. Elizabeth's Hospital in Youngstown, Ohio, where he served a residency; formerly a resident at St. Vincent's Hospital in Jacksonville, Fla., and St. Thomas Hospital in Nashville, Tenn.; in 1952 called into service with the Air Force and served in the Azores; on the staff of the South Florida Baptist Hospital; died in the Veterans Administration Hospital, Bay Pines, Dec. 31, aged 37.

Thomson, Allen Milo, Santa Rosa, Calif.: University Medical College of Kansas City, Mo., 1898; a surgeon in the Navy during the Boxer Rebellion and the Spanish-American War; veteran of World War I; died Dec. 24, aged 82.

Tuohy, Edward Boyce Ⓜ Los Angeles; born in Duluth, Minn., March 17, 1908; University of Pennsylvania School of Medicine, Philadelphia, 1932; interned at the Ancker Hospital in St. Paul; went to Rochester, Minn., on Oct. 1, 1933, as a fellow in medicine at the Mayo Foundation; in 1935 changed to anesthesiology; on April 1, 1935, was appointed a first assistant in anesthesiology and on Oct. 1, 1935, was appointed to the staff of the Mayo Clinic as a consultant in anesthesiology; received the master of science in anesthesiology from the University of Minnesota in 1936; an instructor in anesthesiology in the Mayo Foundation, Graduate School, University of Minnesota in 1937, assistant professor in 1940, and associate professor in 1945; resigned in 1947 and accepted the appointment as professor of anesthesiology and head of the department of anesthesiology at Georgetown University School of Medicine in Washington, D. C.; later appointed clinical professor of surgery (anesthesiology) at the University of Southern California School of Medicine in Los Angeles; specialist certified by the American Board of Anesthesiology and a member of the board of directors from 1950 to 1956; veteran of World War II; promoted to the grade of lieutenant colonel in the reserve corps in 1954; delegate, section on anesthesiology, American Medical Association, 1957-1958, and member of its House of Delegates in 1949, 1952, 1954, 1956, and 1958; past-president of the American Society of Anesthesiologists; member of the International College of Surgeons, American College of Anesthesiologists, California Society of Anesthesiologists, American Society for Experimental Pharmacology and Therapeutics, American Association for the Advancement of Science, the Society of the Sigma Xi, the Alumni Association of the Mayo Foundation, the Nu Sigma Nu and Chi Psi fraternities; on the staffs of St. Vincent's, California, and St. John's hospitals, and the Hospital of the Good Samaritan; served as consultant in anesthesiology to the U. S. Naval Medical Center and the U. S. Public Health Service, and a senior consultant in anesthesiology to the U. S. Air Force; contributed more than 100 papers to the medical literature, chiefly on anesthesia; died Jan. 12, aged 50.

FOREIGN LETTERS

AUSTRIA

Parathyroid Insufficiency in Children.—At the meeting of the Society of Pediatrics in Vienna in December, Dr. H. H. Jesserer stated that although parathyroid insufficiency is rare in children it is of practical significance because of its misleading symptoms. The disease may occur in all stages of life, even in the neonatal period, and it may lead to epileptiform or tetanic convulsions. The epileptiform convulsions occur more frequently and often lead to an erroneous diagnosis. Later retardation of physical development; anomalies of the teeth; morbid changes of the nails, hair, and skin; or a lamellar cataract may develop and point to the correct diagnosis. All these changes can be prevented by the administration of dihydrotachysterol or vitamin D. The prognosis of this disease depends largely on an early diagnosis and appropriate treatment. If, because of an erroneous diagnosis, proper treatment is delayed, irreversible changes of hypoparathyroidal cretinism may occur.

Cervical Biopsies at Delivery.—At the meeting of the Society of Gynecology and Obstetrics in Vienna in December, Drs. V. Gruenberger and R. Ulm reported on cervical biopsy specimens taken from 110 women immediately post partum. These showed excessive hyperemia and edema, marked thinning of the pavement epithelium, hypertrophy of the mucosa, and round cell infiltration. Less than half of the specimens showed a pronounced decidual reaction. In 28 the border of the cylinder pavement epithelium was outside the opening of the cervix located at the margin of a glandular ectopia and in 22 it was within the opening of the cervix, since epidermization extended into the cervical canal. Atypical changes of the pavement epithelium were present in only eight patients. No malignant degeneration of the pavement epithelium was seen. In view of these findings the possibility of an involution of the atypical pavement epithelium up to the end of pregnancy is suggested.

BRAZIL

Wandering Spleen.—In January, at the 20th anniversary meeting of the Sanatorio São Lucas of São Paulo, Dr. E. B. Ribeiro gave a lecture on wandering spleen. He stressed the difficulties of diagnosis as the wandering spleen may occupy any part of the abdominal cavity, where it may be mistaken for a tumor. The patient usually goes to a doctor only when acute torsion develops. A thorough examination is not always possible because the severity of the symptoms may call for immediate operation. In the Brazilian medical literature, only six cases of wandering spleen with torsion of the pedicle have been reported. Dr. Ribeiro's patient (the seventh) was operated on, as generally happens, with the diagnosis of torsion of the pedicle of an ovarian cyst. The patient was a 15-year-old girl who several years earlier received a blow to her left hypochondrium. After that accident and since her seventh year she had been aware of a wandering abdominal tumor. Acute symptoms appeared only when the torsion occurred. When she was examined, a mass was felt in the left lower quadrant of her abdomen, disappearing into the pelvis. This condition is much more frequent in women than in men.

CANADA

Blood Transfusions and Jehovah's Witnesses.—Headline news was recently made by the refusal of members of Jehovah's Witnesses to let their children receive blood transfusions under any circumstances. The controversy is not new but has reached new heights. The current episode began early in November, when the son of a Witness was shot in the leg, lost a lot of blood, and required a blood transfusion as a lifesaving measure. The Children's Aid Society in Manitoba, where permission for this necessary measure was being withheld by the parents, wished to have the boy made their ward because of alleged parental neglect, but unfortunately the legal procedure involved delayed a decision until the boy had died. Soon afterward a lawyer told a panel of physicians that in seven or eight cases he had advised doctors in a similar situation to give a transfusion and risk a court action, since he believed that there was not one chance in 5 million of a doctor concerned being charged with assault. He said that he did not see how anyone could face damages after saving a life. This advice was frowned on by the secretary of the Canadian Medical Association, who pointed out that parents had a perfect right to accept or reject treatment offered, and that it would be difficult for a physician to state categorically that without a transfusion a certain patient would inevitably die. The secretary of the Canadian Medical Protective Association, speaking on the same

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The items in these letters are contributed by regular correspondents in the various foreign countries.

panel, believed that a physician had no right to do anything to a child without the consent of the parent or guardian.

In mid-December this same problem arose in Toronto where at the Hospital for Sick Children a child with erythroblastosis required a transfusion and the parents, Jehovah's Witnesses, refused permission. When the situation had become desperate, a court awarded custody of the infant to the Children's Aid Society. Within four minutes of the announcement of the decision the first transfusion had begun, and the child's condition improved steadily. A plan by the counselor for the Witnesses to appeal the decision to the Ontario Supreme Court was dropped, but the case continued to excite argument in the press, with Bible scholars, ministers, rabbis, and lawyers all giving opinions, and with the likelihood that the precedent set will be followed on future occasions.

Hospital Insurance.—Well over 50% of Canadians are covered by government hospital insurance schemes. In recent months Ontario, which started its compulsory scheme on Jan. 1, enrolled over 90% of the population and introduced some additions to the original plan. For example it was agreed that patients in approved nursing homes would have their bills paid by the plan, and the government intends to use 600 vacant beds in tuberculosis sanitariums for care of chronic and convalescent invalids under the scheme. Moreover, it raised its payments to hospitals for outpatient visits from 30 cents to $1.50, as a measure toward making better use of outpatient departments and relieving the crowding of hospital beds. This is of particular benefit to teaching hospitals, in which costs of running outpatient departments are high (for a Toronto hospital costs are about $3.50 a visit and revenue about $1.30). Hospitals will receive from the government a special depreciation grant for 1959 of $150 per bed against debt retirement, future depreciation, and future expansion. Similar grants have been made in the past, but there was no certainty that they would continue. The aim of the new plan is to encourage hospitals to provide more accommodation.

Dental Services Insurance.—Organized medicine has long recognized the need for some form of insurance for medical care among the less privileged sections of the population and has also held that schemes for the provision of such services will function more efficiently if they are controlled by the profession than if they are controlled by the government. Dentists are now expressing similar sentiments, and at a November meeting the secretary of the Royal College of Dental Surgeons suggested a national health scheme including both medical and dental services. A plan has been operating in Saskatchewan for three-and-one-half years, and is being adapted for use in Alberta and Ontario in 1959, whereby a patient may receive necessary dental care and pay for it in installments without third-party participation. Patients arrange with their dentists about payment over an agreed period and are charged an initial service fee of $1 plus 30 cents a month if the account is under $150. Dentists are charged 1% on accounts remitted and a $35 membership fee. In addition, a welfare plan, with payment by the government, provides basic dental care for dependent children or dependent foster children qualifying under the Mothers and Dependent Children Act of 1957. Payment is at the rate of 70 cents a month for each child involved. The editor of the *Canadian Dental Association Journal* defended such schemes vigorously.

Thrush in Nurseries.—Harris and co-workers (*Canad. M. A. J.* 79:891, 1958) studied thrush (neonatal candidiasis) at the New Mount Sinai Hospital, Toronto, with a view to its elimination from the hospital nurseries. The departments of obstetrics, pediatrics, and pathology cooperated in this study, which involved 1,442 consecutive pregnant patients and their infants. Cultures were made from vaginal smears of all patients before preparation for labor, and cultures were made of oral swabs taken from all the infants on the first or third day and on the day of discharge. The incidence of vaginal candidiasis was 17.6%; oral cultures made from about 20% of the infants of these women were positive; and 11.4% suffered from thrush. Among those women from whom negative cultures were made the incidence of contamination was low. The use of antibiotics or douches was not a factor in contamination, but early rupture of the membranes appeared to have some protective effect on transmission from the vagina to the infant. Breast-feeding did not appear to increase the incidence of infection. Of 714 infants treated prophylactically with nystatin by oral instillation only 0.4% developed thrush, whereas of 728 control infants 4% developed this infection. The dose now recommended is 100,000 units instilled into the mouth on the second and fifth days of life. The last 615 babies so treated have all been free from thrush.

Q Fever.—In 1956, for the first time, a case of Q fever was reported and some time later it was pointed out that a large proportion of the provincial population appeared to have in their blood antibodies capable of complement fixation in the presence of the specific antigen of Q fever. Pavilanis and co-workers (*Canad. Pub. Health J.* 49:520 [Dec.] 1958) reported an epidemic in the little town of Princeville, Quebec, with a population of 2,700, in which over 33% of the workers at the local abattoir were involved (62 cases within 17 days), and nobody else. The illness was at first thought to be a Salmonella infection, but it did not respond to antibiotics, and serum agglutination tests were inconclusive, so the provincial epidemiologist was consulted. The clinical signs were those of an acute respiratory virus infection, and only employees handling the carcasses and viscera of slaughtered animals were affected.

Two teams, one for laboratory testing and another for veterinary investigation, were formed. The laboratory showed by serologic tests that the causative agent was Coxiella burnetii and this agent was also isolated from four sample of ewe placenta. It was also found that 9.9% of the bovine population of the province either was or had been infected with this agent. The sheep of the province were more infected than those in northern California, with a positive incidence of 59% in a series of 91 tested. The sheep parasite Melophagus ovinus seemed to be a vector.

Unions Consider Medical Plan.—On Jan. 15 a conference of Toronto trade union leaders appointed a committee to investigate the possibility of establishing a new medical care program, after union welfare experts had criticized existing medical plans as inadequate and recommended instead a group practice plan with salaried physicians as the most desirable type. The union specialists particularly criticized the major medical plans underwritten by commercial carriers. One spokesman said, "With the deductible and co-insurance features of these plans, we would estimate that the average Toronto trade unionist and his family would be paying the greater share of their medical costs out of their own pockets." He believed that there was insufficient emphasis in current plans on the maintenance of health or the prevention of illness. Although the federal-provincial hospital plan was praised, the absence of outpatient coverage was lamented. A deadline of 18 months has been set by the conference for a report and a second conference to put the program into effect. The idea is presumably to get a pilot scheme going in Toronto as a model for more widespread plans later.

Traffic Accidents.—A pilot study of persons injured in traffic accidents who were treated in the Montreal General Hospital and the Montreal Children's Hospital in a six-month period was made by Ruth McDougall (*Canad. M. A. J.* 80:18, 1959). Although this study could not be taken as representative of accidents in the city as a whole, since only 8.3% of all injured came to these two hospitals, it revealed the basic ignorance surrounding these common occurrences. While more passengers were treated than drivers, statistics do not show whether the passenger is in greater danger than the driver since the police do not keep figures for total passengers in such accidents. Although the risk to pedestrians appears to be greatest among the very young and the very old, there is no percentage estimation of the risk in these age groups. The commonest type of accident was a collision between two vehicles, and the greatest number of accidents occurred between midnight and 4 a. m., but no figures for traffic density by four-hour periods are available.

Of 294 such patients treated at the Montreal General Hospital 79.3% were treated as outpatients and 20.7% were admitted. Of the outpatients it appears that 43.5% did not really need hospital services. Only three fractures (fibula, maxilla, and a cervical vertebra) were missed. Of the 294 patients 1.2% had fatal, 19.8% serious, and 79% minor injuries. Only four patients were left with a permanent disability. Whereas among those 15 years of age or over only 31.1% were pedestrians, 77.4% of the children under 15 were pedestrians. The need for uniform accident reporting across Canada is stressed, so that areas of high incidence can be compared with those of low incidence.

Homosexual Transmission of Syphilis.—Early in 1957 the increase in infectious syphilis noted in other parts of Canada and the United States suddenly became evident in British Columbia, and it was found that increasing numbers of male patients at the venereal disease clinic in Vancouver were admitting to male contacts. There had been an epidemic of venereal disease in this area among homosexuals in 1951. In 1957, 77% of men treated for early syphilis in Vancouver clinics admitted homosexual activity, and there were a number of cases of gonorrhea as well. In reporting this significant change in disease pattern Larsen (*Canad. M. A. J.* 80:23, 1959) pointed out that homosexuals with venereal disease appear to be more promiscuous than their heterosexual counterparts and are therefore a greater potential menace. It is also likely that some contacts are being missed by private practitioners. The most effective method of dealing with this situation lies in the examination of the greatest possible number of contacts, which depends on cooperation of the patients.

Pneumocystic Pneumonia.—While over 2,000 cases of pneumonia due to Pneumocystis carinii have been reported from Europe, the total in the Canadian literature now stands at only 23. Berdnikoff (*Canad. M. A. J.* 80:1, 1959) recently described 14 cases from Montreal, giving full details for the last 3 in his series. He noted that the age incidence lay between 2 and 4 months, and that about 40% of cases were in premature infants. Debility due to previous infection or neurological disease seemed to be an important factor, and in each patient the illness started suddenly with periods of dry unproductive cough and signs of suffocation. Oxygen usually brought temporary relief to the cyanosis and tachypnea. There was no fever. A diagnostically significant feature may be the occurrence of a symptom-free period of a few days after the onset of the disease, which was observed in seven of the author's patients. Auscultatory signs were usually absent, though pneumothorax was not rare. Leukocyte counts and roentgenograms were diagnostically unreliable. All the 14 patients in this series died, although some patients are reported to have recovered. In the same issue (*ibid.* 80:35, 1959) Junger and Wyllie of Montreal report another case of pneumocystic pneumonia that was diagnosed during life, in a 3-month-old premature child with brain damage. A chest roentgenogram was recognized by a European physician as typical of interstitial plasma cell pneumonia due to this organism. The child was cyanotic but without fever or abnormal physical signs in the chest. Death the next day led to autopsy confirmation of the diagnosis.

DENMARK

Bronchial Asthma in School Children.—Sven Fransen (*Acta Allergol.* 12:341-357, 1958) reported that for the school year 1949-1950 an incidence of bronchial asthma of 0.8% was found among school children in Copenhagen. The incidence was highest at ages 9 to 12 years. Over 33% were girls. The frequency of nonattendance increased gradually with the intensity of the disease. Many children had a high frequency of nonattendance, and about 20% had been absent from school for more than a quarter of the school year. With regard to knowledge, the children did well in spite of prolonged nonattendance; almost 33% were above average and less than 17% below. Over 25% of the boys and almost 50% of the girls were wholly or partly excused from physical exercise and sports. Chronic sequelae of the asthma in the form of deformity of the thorax, emphysema, and faulty carriage were seen in 17%. About 25% had not been referred for specialist treatment of the disease and the author considered that there was insufficient treatment of this disease among school children.

Epilepsy in Children.—Dr. S. Brandt (*Nordisk medicin*, Jan. 15, 1959) reviewed his experiences with 100 epileptic children who, after treatment in hospital, had been kept under ambulant observation. He studied their reactions under home conditions, noted the choice and dosage of drugs, kept a look-out for symptomatic epilepsy with a view to rendering air-encephalography unnecessary in some cases, and attempted by systematic blood counts to avoid untoward drug reactions. The epilepsy was symptomatic in 16 patients, cryptogenic and nonfamilial in 54, and cryptogenic but possibly familial in 30. In 30 the epilepsy had begun before the age of 2 years. Using the frequency of epileptic attacks as an index, the results of ambulant treatment were as follows: 53 were free from attacks, 19 were improved, and 28 were unchanged. These findings were, on the whole, confirmed by electroencephalography. The outlook appeared to be best for the children with symptomatic epilepsy and worst for those with defective intelligence and subject to different types of attack. Some of the children suffering from petit mal relapsed even after an interval of several years' freedom from attacks.

Can Routine Blood Counts Prevent Drug Reactions?—In *Ugeskrift for læger* for Jan. 15, Dr. T. K. With questioned the value of blood counts in the prevention of agranulocytosis, and the thrombopenias and hemolytic anemias induced by drugs. His scrutiny of the history of blood counts in this connection failed to reveal any solid basis for them, and it is significant that there is as yet no unanimity over the procedure to be followed. A craving to insure against a hematological mishap has made many take refuge in a laboratory test which has become hallowed by usage. It is not only of doubtful value, but may also create a false sense of security. Clinical control based on the vigilance of the patient is the only effective measure. At every consultation he must be reminded of the risk involved in taking the drug in question, and he must discontinue it at once and consult his physician on the development of fever, malaise, sore throat, or a rash. The physician may then arrange for a differential white blood cell count and, if necessary, he may repeat it frequently for about two weeks after withdrawal of the drug. Routine serial blood counts per se, however, are of such doubtful value and cause so much inconvenience to patient and laboratory that, in With's opinion, they should be abandoned entirely.

New Succinimide for Petit Mal.—The new succinimide, PM 680, was tested by Trolle and Kiörboe (*Nordisk medicin*, Dec. 11, 1958) for 16 months at the Rigshospital in Copenhagen and the Odense City Hospital on 34 children (aged 3 to 15 years) and 4 adults suffering from petit mal attacks or allied conditions. Among them were six who also suffered from grand mal attacks. The usual initial dose was one 250-mg. capsule of the drug once a day. Every second or third day the dosage was increased by 250 mg., and for children between 10 and 12 it was usually 2 Gm. daily, given in three doses during the day. In some patients the dosage was much higher without definite side-effects. In some it took several months to determine the optimal dosage. Fourteen patients were completely relieved of their attacks, and classification of the patients according to the duration of their ailments showed that those fared best whose illness had lasted less than five years. The four adults did not fare well. Electrocardiograms in 6 of 37 patients became normal and in 18 showed marked improvement. A good correlation was established between the electrocardiographic and clinical findings. There were no side-effects necessitating withdrawal of the drug, and no abnormal changes developed in the blood periodically submitted for leukocyte counts. In addition to the 14 patients who became seizure-free, 17 showed a 50 to 99% reduction in seizure frequency. Only seven showed no improvement. In several patients the drug was found to be superior to earlier succinimide preparations and to produce fewer undesirable side-effects.

Surgery in the Elderly.—In 1946, the proportion of the population of Copenhagen aged 70 years or more was 4.8%. In the same year, 3.6% of the patients in department A of the Bisperbjerg Hospital were in this age group. There were thus fewer elderly patients than might be anticipated from the age distribution of the population. Ten years later the situation was reversed. The elderly inhabitants had risen to 6.8% and the number of such patients in hospital had risen to 9.2%. As a result, hospital mortality has risen. In the same decade the number of hospital patients over 70 and regarded as operable had risen from 25 to 50%, according to Dr. E. Amdrup and co-workers (*Danish Medical Bulletin,* December, 1958) who noted that twice as many of these patients are now operated on as were so treated in 1946 and the operative mortality has fallen. It must be anticipated that more and more patients over 70 will require operation. Indeed it would seem that old age is now hardly ever a contraindication per se for surgical treatment.

GERMANY

Iron-Binding Capacity of the Serum.—Lange and Oberhoffer (*Deutsches Arch. klin. Med.* 204:697, 1958) stated that the serum iron plays an important role in the differential diagnosis of diseases associated with jaundice. Clinical trials were conducted to determine the iron-binding capacity (FeBC) of serum in hepatic disease and in health. The test included 60 patients with hepatitis (maximum icterus), 26 with hepatic cirrhosis, 25 with obstructive jaundice, and 60 healthy controls. Uncomplicated acute hepatitis was found to be characterized by marked hypersideremia. The maximum FeBC was also increased in most patients, although less markedly. The latent FeBC was below normal. The serum iron level was below or within normal limits in most patients with obstructive jaundice. The maximum FeBC was reduced and the latent FeBC was normal in 17 of the 25 patients.

In those with cirrhosis, the serum iron pattern was irregular. There were normal as well as lowered and slightly increased values. The maximum FeBC was usually markedly lowered and the latent FeBC was reduced in 23%. The pattern of these values may be of diagnostic and, perhaps, prognostic importance. Intercurrent infections may give misleading values, as these processes are not liver-specific. The observed increase of maximum FeBC in patients with hepatitis has not yet been explained. The decrease of FeBC in chronic diseases may be due to disturbance of transferrin synthesis. In acute breakdown of hepatic function, a marked decrease of FeBC may occur, which may explain the abrupt fall of the serum iron level.

Parathyroid Tetany.—Tetany not only consists in spasm but also in other symptoms included in the term latent tetany. The serum calcium level in parathyroid deficiency is important. The fact that most tetanic patients have normal blood calcium levels (69 of 71 patients) gives rise to the question of whether these patients also have a parathyroid deficiency. K. W. Essen (*Deutsches med. J.* 9:410, 1958) believes that a subthalamic tetany center, which directs neuromuscular excitability of the periphery, may be excited by hypocalcemia (parathyroid deficiency) as well as by alkalosis (hyperventilation or loss of chlorine and acid), organic cerebral lesions, and constitutionally or dispositionally lowered excitability threshold (tetanic manifestations after stress).

The acute tetanic attack can be interrupted by the intravenous injection of a simple calcium salt, but complex calcium salts have not proved effective. For long-term treatment of hypocalcemic tetany, dihydrotachysterol and vitamin D are useful, while injections of parathyroid hormones are superfluous. In contradistinction to other authors, Essen concluded from the good results he obtained that dihydrotachysterol should also be used to treat normocalcemic forms of tetany in order to compensate a partial parathyroid deficiency (without hypocalcemia), to correct an alteration of the acid-base equilibrium of central origin, and to correct the ultrafiltrable serum calcium.

Prednisone for Tuberculosis.—H. D. Renovanz (*Ärztl. Wchnschr.* 13:805, 1958) attempted to determine in vitro and in vivo, whether an alteration of sensitivity occurs in resistant strains of Mycobacterium tuberculosis under the effect of cortisone and its derivatives. He found that there are no differences in the type and course of tuberculosis between sensitive and resistant strains and that no alteration of sensitivity of resistant strains occurs. He treated 50 tuberculous children and adolescents under tuberculostatic protection with prednisone. Marked improvement was achieved in 27 and complete radiologic remissions occurred in 8 of these. The condition remained unchanged in seven, and in five only the more recent, inflammatory perifocal patches receded. In the others there was a distinct aggravation of the disease. In one patient a reactivation occurred during treatment and in five others it occurred four to eight weeks after termination of treatment. Adjuvant treatment with steroid hormones is recommended for extensive tuberculous changes of recent origin in childhood and adolescence if the tuberculous changes have proved resistant to specific therapy. With a dosage of 10 to 20 mg. daily for 45 days, which is gradually withdrawn with the use of ACTH, nonspecific side-effects are not to be expected. Prerequisites are adequate tuberculostatic protection and regular clinical and radiologic controls to detect any new activation early.

Antibacterial Substances in Tissue.—H. Stein (*Beitr. Klin. Tuberk.* 118:314, 1958) stated that the body fights invading microorganisms mainly by serum antibodies and phagocytes. Interest is further attached to the question of how far antibiotic powers of the tissues play a role in combating various pathogens. The author's studies showed that liver tissue possessed remarkable bactericidal powers against Staphylococcus pyogenes var. aureus and Pseudomonas aeruginosa, while distinct inhibition or destruction of Escherichia coli was rare. There were marked differences in antibacterial activity in the liver from various mammals. Although the role of the individual factors relative to the whole antibacterial defense mechanism has not yet been fully explained, the author's investigations indicate that the body is capable of developing antibacterial substances that are comparable to antibiotics.

Vitamin A and the Pancreas.—M. Gülzow (*Ärztl. Wchnschr.* 13:597, 1958) reported that vitamin A deficiency may result from absorption disorders in pancreatic disease associated with digestive insufficiency, but it is rare in adults. Intraduodenally or intramuscularly administered vitamin A in doses of 40,000 units elevated pancreatic secretion. An excretory function test largely confirmed the stimulation of secretion, which occurred in two phases. Parallel with the secretory impetus there was frequently an enzymatic derangement. Examination of the serum diastase after intramuscular injection of vitamin A in 93 persons revealed fluctuating values not only in patients with pancreatitis but also in those with hepatic disease, diabetes, epigastric disease, and some without epigastric disease but with disturbance of equilibrium. In clinically proved pancreatic disease, on the other hand, the reaction sometimes fails to occur. In health the serum ferment reaction was less frequent (16%) when 210 tests, using mecholyl, were made. These tests suggested abnormal pancreatic function. Vitamin A, stimulating pancreatic secretion, is indicated for the treatment of subsiding acute pancreatitis. The mild pancreatic sialorrhea was considered as advantageous as the bile-flow in certain hepatic diseases.

Cancer Caused by Arsenic.—Occupational contact with insecticides and fungicides containing arsenic and the use of arsenic for certain skin diseases and anemia often cause cancer of the skin and internal organs. W. Braun (*Deutsche med. Wchnschr.* 83:870, 1958) reported a series of 16 vine-growers who handled large amounts of arsenic-containing insecticides between 1925 and 1942. Those who had drunk wine regularly developed nine inoperable bronchial carcinomas, three cases of epidermoid carcinoma, one carcinoma of the bile duct, one malignant tumor of a cervical lymph node, and three prickle-cell cancers of the skin, in addition to typical arsenical keratoses. The author also observed two cancers resulting from arsenical treatment. He further reported on three vine-growers with cancer of the lung, not presenting with cutaneous symptoms, after the use of arsenic, and 14 vine-growers with cancer of various organs in whose case histories contact with arsenic was not recorded but had probably taken place. Braun agreed with other authors than arsenic is a dangerous cancerogenic agent and that only in exceptional cases should a physician prescribe it.

Side-effects of Antibiotic Treatment.—H. Dennig (*Deutsche med. Wchnschr.* 83:1849, 1958) reported that of 170 patients treated with penicillin 5 cases of allergic exanthema occurred. Streptomycin caused one local reaction in a series of 50 patients. No vestibular or cochlear damage was observed. Streptomycin and penicillin combined gave rise to 6 cases of allergic exanthema in a series of 220 patients. The symptoms subsided after withdrawing the drugs. Of 117 patients treated with tetracycline, 1 case of exanthema and 6 of diarrhea occurred. Of 50 patients receiving chloramphenicol, 2 developed exanthema, 2 diarrhea, and 1 a fungus infection which may have been responsible for the patient's death. Erythromycin was given to 30 patients and was well tolerated by all. Of 11 patients receiving oleandomycin, only 1 complained of nausea. Of 76 taking tyrothricin inhalations, only 1 had an itching exanthema, which disappeared after administration of soventol and calcium. Dennig concluded that serious side-effects occur only in the form of enterocolitis (5% of those treated with tetracycline and 4% of those treated with chloramphenicol). Penicillin shock, severe dermatitis, and aplastic anemia were not seen in these series. The author emphasized that the drawbacks of antibiotic therapy are negligible when compared to the advantages.

NORWAY

Antistaphylolysin in Children with Asthma.—Harnaes and Borgen (*Acta Allergol.* 12:336-340, 1958) determined the antistaphylolysin titers of 113 asthmatic children. Elevated values were significantly more frequent than in the 58 nonasthmatic patients in the same age range who were used as controls. The skin-negative patients suffering from asthma of supposed bacterial origin and the truly allergic skin-positive children did not differ significantly, but a tendency toward increased values was noted in the former. The authors considered the possibility of an increased antibody-producing tendency per se among the allergic children.

SWEDEN

Lupus Erythematosus.—C. Ekelund (*Acta rheumatol. scandinav.* 4:172-177, 1958) examined 226 persons and found the gamma globulin to be increased in all those who showed a fairly strong positive reaction to the *p*-toluenesulfonic acid test, but the gamma globulin was found to be increased also in several of those who gave a negative or only weakly positive reaction. Ekelund stated that clinically the patients with a strongly positive reaction were often found to have either systemic lupus erythematosus or florid rheumatoid arthritis. Of 10 with L. E. cells the test was either negative or only weakly positive in 5, while in 165 patients with rheumatoid arthritis the reaction was positive in 55, though usually only weakly positive. False-positive reactions were also obtained in patients with myeloma and those with hepatic cirrhosis. The test cannot be regarded as a reliable tool for differentiating between lupus erythematosus and rheumatoid arthritis. The author concluded that perhaps there is no sharp border between these two diseases.

Steroids for Asthma.—Hans Arnoldsson (*Acta allergol.* [supp. 6] 12:1-190, 1958) reported that between January, 1953, and June, 1958, about 1,000 asthmatics were treated at the Allergy Clinic in Gothenburg, Sweden. Of these 161, with an average age of 54 years and a mean duration of asthma of 15 years, had endogenous bronchial asthma of such severity and intractability that corticoid therapy was considered essential. The patients were treated with ACTH and corticosteroids and given suitable bronchodilators and expectorants. The response to this preliminary course was excellent in 65.2%, good in 25.5%, and poor in 9.3%. Other forms of treatment were applied as a control measure to 26 and 43 received a placebo instead of prednisone. In two control series, comprising 69 patients, a recurrence of asthma of a degree requiring resumption of corticosteroid therapy occurred within four weeks in 40.5% and within eight months in 98.5%. To the treated series of 92 patients, 63 transfers were added from the control series and 11 were lost to the study. At the end of the investigation the longest duration of therapy was almost six years and the shortest 8 months (average 25 months). The response to therapy as judged by its effects on the severity of the asthma, working capacity, and relapse rate varied from good to excellent. At the end of the investigation 37.5% of the patients were free of asthma, 42.3% had mild symptoms occasionally, and 20.2% had moderate to severe asthma. Before therapy 89.5% of the patients had severe asthma and 10.5% moderate asthma.

The incidence of salicylate hypersensitivity among the patients in the treated series was 18%. The clinical response to long-term corticosteroid therapy of the salicylate-sensitive patients was favorable and they seemed no more resistant to such therapy than any other patients with bronchial asthma. Side-effects were cardiac and circulatory disturbances, aberrations of water and electrolyte metabolism, neurological and psychiatric manifestations, peptic ulcer, allergic reactions to ACTH, osteoporosis, and adrenocortical hypofunction. Seventeen patients between 48 and 78 years of age had signs of myocardial disease before the commencement of therapy, and some required maintenance doses of digitalis. Four of them had a myocardial infarction, but while therapy was in progress cardiac diseases definitely attributable thereto were not seen in any of these patients.

More than 800 determinations of serum sodium and potassium levels were made. About 96% of the sodium levels and more than 99% of the potassium levels were within the normal range. Weight increases, frequently marked, were common. Most of these increases could be ascribed to improved appetite resulting from better general health and a sense of well-being accompanying relief from symptoms. The author concluded that ACTH or corticosteroids could be given in minimal effective doses for several years without sodium restrictions or supplementary potassium. The so-called withdrawal syndrome was not observed, and the adrenal cortex responded adequately to various stressful stimuli without special therapy other than extra cortisone before and after major operations. Considering that 89% of the patients with osteoporosis were postmenopausal women, it seemed advisable to provide adjuvant treatment with a combination of androgens and estrogens for such patients on long-term ACTH or corticosteroid therapy.

Hypersensitivity to Phenylcarbinol.—B. Lagerholm and co-workers (*Acta allergol.* 12:295-298, 1958) were unable to find any report of hypersensitivity to phenylcarbinol used as a preservative in vitamin B_{12} solutions for injection. They observed a 28-year-old patient with arthropathic psoriasis who was given a course of vitamin B_{12} injections. The preparation contained 15 mg. of phenylcarbinol per milliliter as a preservative. Both the skin and the joint changes responded favorably, but after some time a regression occurred with increased joint distress, itching, pronounced reddening of the psoriatic lesions, and urticaria. Repeated thrombocyte tests with the selected brand of vitamin B_{12} made the platelet count drop heavily, from 439,000 to 45,000 in 60 minutes. Subsequently the patient underwent a course of treatment with pure, unpreserved vitamin B_{12}. This produced no untoward reactions. The negative thrombocyte test with pure vitamin B_{12} and the absence of untoward reactions while the patient was receiving pure vitamin B_{12} constituted further evidence that phenylcarbinol was the causative agent.

Asian Influenza.—An epidemic of Asian influenza occurred in Sweden in the period September, 1957, to April, 1958, with the peak morbidity in November, 1957. B. Körlof and co-workers (*Nord. med.* 60:1704-1706 [Nov. 27] 1958) estimated that about one million persons were affected, the highest incidence being reported among school children and Army personnel. The number of deaths from the influenza or its complications was highest in children below the age of 16 years and in persons over 61. The cause of death in most cases was pneumonia. The bacteria most commonly found in the lungs on autopsy were Staphylococcus pyogenes var. aureus and Escherichia coli.

Leo Heller and co-workers in the same issue reported that the antibody responses of volunteers inoculated with decreasing dilutions of a monovalent formalinized Asian influenza vaccine, prepared at the State Bacteriological Laboratory in Stockholm, were determined by the hemagglutination-inhibition test. In spite of the low hemagglutinating capacity of the vaccine strain (A/Singapore/1/57) even extremely small doses of the vaccine gave 11 to 22% serologically positive results after one and 55% after two injections. A dose of 1,500 hemagglutination units produced an antibody response after one injection in almost all subjects. Another vaccine preparation with a high hemagglutination titer was tested in a field trial on more than 1,000 recruits in an attempt to perform a direct titration of the protective effect of the vaccine. The protection rates found for doses of 2,000 hemagglutination units each were 69 to 86% for two and 57 to 78% for one injection. The corresponding figures for doses of 400 hemagglutination units each were 45 to 54% protection after two doses and 29 to 45% after one.

Proton-Beam Therapy.—Prof. L. Leksell and co-workers of the Gustaf Werner Institute for Nuclear Chemistry at Uppsala described the destruction by proton irradiation of a small cerebral tumor in a man aged 54. A beam of protons from a synchrocyclotron was focused on the tumor after its careful spatial localization by elaborate stereotaxic methods. Protons, unlike electrons and roentgen rays, are not widely scattered in the tissues, and as they give up their energy on reaching their target their effect can be localized to a small, preselected area of tissue. The procedure, being painless, required no anesthetic. The patient's head, which was fixed by clamps, was rotated for each exposure so that the proton beam could strike the target area from different angles. Forty exposures, each lasting 30 seconds, were given. The position of the tumor relative to the path of the beam was checked after each exposure to prevent normal brain tissue from being damaged. The patient was 80 ft. from the synchrocyclotron, from which he was separated by two 6-ft. walls. The beam was led from the synchrocyclotron through a tube 60 ft. long passing through the walls and focused by four lenses. The authors directed operations from a control room in which the patient was seen on a television screen, and they communicated with him by means of a microphone system. These elaborate screening precautions were necessary to prevent excessive radiation reaching the patient and the operators.

UNITED KINGDOM

Gastrotonometry.—In the course of treatment in a respirator it is essential that ventilation be controlled by adjusting the apparatus from time to time. The best guide to control is the carbon dioxide tension (pCO_2) of arterial blood, the determination of which involves arterial puncture and special blood storage. From studies made on over 400 patients in respirators Boda and Muranyi (*Lancet* 1:181, 1959) concluded that the pCO_2 of arterial blood could be deduced with reasonable accuracy from the intragastric pCO_2, which they found runs parallel to it and is usually 2 to 4 mm. Hg higher. For the determination of the intragastric pCO_2, termed gastrotonometry, they introduced through the nose into the stomach a thin-walled rubber balloon under 0.05 mm. thick and attached to polyethylene tubing. Not less than two hours after the last meal the balloon is filled with 20 ml. of room air through the tube, which is then sealed off. Gas in the stomach diffuses into the balloon. After equilibrium is established (about two hours) the air is sucked from the balloon into a suitably oiled syringe and its pCO_2, as well as that of the expired air, is measured by an infrared absorption method.

The authors found that in hyperventilation the gastric pCO_2 decreased, while in hypoventilation it increased. When ventilation was adequately adjusted, and there was no respiratory complication, the gastric pCO_2 was close to but a little higher than that at the end of respiration. In hyperventilation and in the presence of respiratory complications the difference between the gastric pCO_2 and that at the end of expiration increased. During treatment pCO_2 measurements indicated the onset of pulmonary complications. Gastrotonometry was found to be a simple and reliable method for the routine control of artificial respiration, particularly for patients being nursed in a respirator.

Pneumonoconiosis.—The National Coal Board's chief medical adviser announced that every British miner will be entitled to have a roentgenogram of the chest at least once every five years. The Board has purchased nine mobile x-ray units as part of its campaign against pneumonoconiosis in miners. It is expected that as a result of improved diagnosis the reported incidence of pneumonoconiosis will rise, but after the introduction of measures to suppress the disease such reported incidence should fall.

Television and the Child.—The rapid growth of television in the last 10 years has evoked much controversy over its effects on children. In 1954 Dr. Hilde Himmelweit and co-workers investigated the problem on behalf of the Nuffield Foundation. Their findings have been published in a booklet entitled "Television and the Child." They found that most children, unlike many adults, viewed selectively an average of about 12 hours of programs weekly. Other mediums of entertainment, such as cinema and radio, tended to suffer in competition. It was found that the more intelligent the child the less time he spent watching television at the expense of other pursuits. Television made less impact on those children leading a full and active life. The child television addict was typically one with personality problems, shy, poorly adjusted, insecure, and handicapped in emotional relationships. Television offers an escape from poor social adaptation, but it creates a vicious circle, because the more these withdrawn children watched it the less they were encouraged to overcome their emotional difficulties. Excessive viewing was the result of personality defects rather than the cause of them. For the correctly oriented child, games, hobbies, and social pursuits retained their attraction and television took second place.

It is difficult to know what effect television has on the child's mind. As many as 75% in the sample voted in favor of adult programs, particularly plays dealing with crime. Westerns were popular. They evoked little anxiety or aggression in spite of their usual background of violence, which is generally stereotyped. Adult plays depicting violence and conflict in human relations were more likely to make an unfavorable impact on the child's mind. Dr. Himmelweit considered that parents as well as television producers have a duty in controlling what the child sees. The investigation showed that television had little effect on the sleep pattern of the average child by causing overexcitement, anxiety, or keeping late hours. Emotionally insecure children might be affected, as they would be by the cinema. Really late bedtimes were no more common among child viewers than among child nonviewers. The inquiry also discredited the popular misgivings about television as a cause of listlessness, morning tiredness, and lack of concentration at school. Television even stimulated interest in reading in some children. Television was not found to make children more passive. No loss of initiative or dulling of the imagination was observed. It did, however, stimulate passive rather than active interests.

Smoking and Disease.—Most examinations of the association between smoking and disease are based on a comparison of the smoking habits of persons who have a specific disease with those of a control group. This procedure has been criticized on the grounds that the controls, however carefully selected, might not be strictly comparable. To overcome this objection Edwards and co-workers examined smoking habits and diseases present in a representative sample of the population (*Lancet* 1:196, 1959). In this way it was possible to compare the incidence of specific diseases in smokers and nonsmokers, rather than the frequency of smoking in affected persons and controls. A medical examination and interrogation of the smoking habits of 1,737 men over the age of 60 years was made. It was found that with increasing age the proportion of cigarette smokers decreased (from 55% in the men aged 60 to 64 years to 22% in those aged 85 and over), with a corresponding increase in the proportion of pipe smokers (from 12 to 50%). At the same time the total amount of tobacco smoked either as cigarettes or in pipes decreased with increasing age. Men of professional and related occupations smoked less than unskilled workers.

Data were obtained on eight of the commonest diseases or disabilities: defective hearing and vision, hypertension, chronic bronchitis, coronary artery disease, arthritis, peptic ulcer, and hernia. Of these hypertension, bronchitis, and peptic ulcer were found to be consistently associated with smoking habits. Hypertension, defined as a diastolic pressure above 100 mm. Hg or a systolic pressure above 200 mm. Hg, was commoner in nonsmokers than in smokers. In the case of cigarette smokers the incidence was inversely related to the number of cigarettes smoked daily. The frequency of hypertension in pipe smokers was intermediate between that of cigarette smokers and nonsmokers. On the other hand the incidence of bronchitis and peptic ulcer was higher in cigarette smokers than in pipe smokers or nonsmokers. The frequency of both diseases increased with the numbers of cigarettes smoked. Both diseases were commoner among men in poorly paid than in well paid occupations, but the effect of smoking appeared to be independent of social class. In all social classes the risks of chronic bronchitis and peptic ulcer were substantially increased by smoking, particularly cigarettes. For all social classes the incidence of peptic ulcer was higher in cigarette smokers than in pipe smokers and nonsmokers.

Unilateral Amblyopia.—Dr. R. Cole of Nottingham found unilateral amblyopia, colloquially known as lazy eye, to be present in 537 of 10,000 National Health Service patients (*Brit. M. J.* 1:202, 1959). In 1% of all patients examined one eye was blind, and in another 2% vision was so poor as to be useless. Amblyopia was considered to be present if visual acuity was less than 6/12 in the absence of disease. It was classed as unilateral if the other eye could read the letters two lines further down the Snellen chart than the amblyopic eye. Translated into general terms the findings suggested that of every 1,000 children born 53 fail to develop normal binocular vision. The left eye was more often involved than the right. Unilateral amblyopia often goes unnoticed until the good eye is affected by disease or injury or until the patient's vision is thoroughly examined.

The higher the intelligence of the patient and the more skilled his occupation, the greater the disadvantage of a nearly blind eye and lack of stereoscopic vision. Unilateral amblyopia results in a great waste of man power. Its economic and social disadvantages are equally serious, particularly if anything happens to the sound eye. Unfortunately the condition develops in infancy and early childhood and may be permanently established by the time the child starts school. Amblyopia primarily affects form vision but not the perception of light or its location, and for this reason it often goes unnoticed. The only way to attack this disability is to examine all children early and regularly and not wait until they go to school.

Dexamethasone.—Metabolic studies on dexamethasone, a new cortisone-like hormone, were made by Slater and co-workers (*Lancet* 1:173, 1959). This drug has been reported to have greatly increased anti-inflammatory action with less disturbance of carbohydrate metabolism than cortisone produces. Patients receiving it were given specially prepared diets of known composition. Fasting blood samples were taken twice a week for electrolyte, sugar, urea, plasma protein, calcium, and cholesterol level estimations, and daily urine and weekly fecal collections were made. Estimations were made of fecal sodium, potassium, nitrogen, and calcium levels, and urinary protein and creatinine levels. After a suitable control period 1 mg. of dexamethasone was given to the patients every six hours. In addition, adrenal suppression studies were made on normal subjects. It was concluded that dexamethasone did not produce sodium retention, but in some patients it greatly increased cell catabolism, with negative potassium and nitrogen level balance. Its action on calcium metabolism appeared to differ from that of cortisone and prednisone, and it was suggested that it should not be used to treat patients with hypercalcemia. The adrenal-suppressing and diabetogenic actions of dexamethasone were comparable to those of cortisone and other currently used steroids. There appeared to be no justification for claims that it is free from side-effects. The clinical effect of dexamethasone was variable in patients suffering from the nephrotic syndrome.

Sex Reversal in the Newborn.—The detection of sex reversal in apparent males has been facilitated by the sex chromatin test. Moore attempted to estimate its incidence by determining from oral smears the chromosomal sex of infants born in a large general hospital (*Lancet* 1:217, 1959). Smears from 3,715 babies—1,911 boys and 1,804 girls—were prepared by scraping the oral mucosa with a sterile nickel spatula, smearing on a slide, fixing with ether and alcohol, and staining with cresyl violet. Of the 1,911 anatomically male infants tested 5 showed female-sex chromatin in the cell nuclei. The anatomic sex was unknown to the observer who examined the slides. The pregnancies of the mothers of these infants were normal, the external genitalia were male in appearance, and the testes had descended. The proportion of nuclei counted in the smears establishing female-sex chromatin varied from 53 to 64%, which is within the range found in the nuclei from anatomically normal girls. All the 1,804 girls were confirmed as genetic females.

The five apparent boys with female-sex chromatin were regarded as cases of female-to-male sex reversal. The incidence was 0.26%, which would correspond to about three cases in every general practitioner's list. Moore suggested that there may be an abnormal metabolism of maternal or placental hormones during pregnancy, resulting in the formation of hormones with an androgenic action. If this occurs early enough they might cause the indifferent gonads of female embryos to develop as testes, with masculinization of accessory sex organs.

Ferguson-Smith examined the frequency of female-sex chromatin-positive micro-orchidism in 663 prepubertal boys attending schools for the [illegible] (*Lancet* 1:219, 1959), which was 1.2%. It is well known that a mental defect is often present in cases of female-to-male sex reversal. In all the cases seen testicular biopsy showed tubular hyalinization and a great reduction in spermatogonia.

CORRESPONDENCE

PHYSICAL FITNESS

To the Editor:—An article "Role of Pediatrician in Physical Fitness of Youth" by Lane appeared in THE JOURNAL (169:421-427 [Jan. 31] 1959). Just as any minister is against sin, any physician is in favor of physical fitness. Many of us deplore the overemphasis which has been placed on this segment of fitness in the last several years and still more resent the implication that the Kraus-Weber tests are a measure of anything more than some functions of a few muscle groups. At the Fort Richie meeting of the President's Citizens Advisory Committee on the Fitness of American Youth, the Special Interest Work Group on Health Services overwhelmingly voted down the suggestion that the Kraus-Weber tests, or any other available tests, could be taken as a scientific measure of "fitness." I question the advisability of reactivating this controversial question when the emphasis on the physical is just beginning to subside to its proper level.

I would like to emphasize that I strongly approve of physical education and think a properly organized program should exist not only in every school but also in every home. The organization of such programs should include recognition of the physiological needs of the persons involved and not be based on chronological age, as is so often the case.

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THE STARCH TOLERANCE TEST

To the Editor:—An article by Nugent and Millhon, entitled "Clinical Evaluation of the Starch Tolerance Test," which appeared in THE JOURNAL (168:2260-2262 [Dec. 27] 1958), deserves comment. This test was proposed by Althausen and Uyeyama (*Ann. Int. Med.* 4:563-575 [Sept.] 1954) for the diagnosis of pancreatic disease. They used soluble starch as prepared by Lintner. Nugent and Millhon used both soluble starch and corn starch. Both are practically raw starch. The mixture is most unpalatable. The maximal rise in blood sugar level after the oral ingestion of 100 Gm. of glucose was compared to the rise after the oral ingestion of 100 Gm. of starch, and conclusions were drawn from the difference. In some cases paradoxical results were obtained. In one patient in whom the pancreatic duct was completely obstructed the test gave negative results. In another patient in whom the proximal two-thirds of the pancreas was normal, the test was strongly positive.

This test has one serious defect, namely, the use of raw or partially boiled starch. This is strikingly illustrated in the observations of Rosenthal and Ziegler (*Arch. Int. Med.* 44:344-350 [Sept.] 1929). They found that equal amounts (50 to 75 Gm.) of well-cooked starch (potatoes) and dextrose produced identical blood sugar curves, but orally administered soluble starch, also prepared according to Lintner, produced no rise in the blood sugar level of normal persons or diabetics. This is not to say that raw starch is not completely digested in the human intestinal tract. Studies of stools after the ingestion of uncooked starchy foods showed that the digestion of starch was complete. The time of digestion, however, was decidedly prolonged.

For this test to have validity, well-cooked starch should be used. Thus, in another study (Wishnofsky and Kane, *Am. J. M. Sc.* 189:545-550 [April] 1935), the starchy food given was thoroughly cooked or baked and consisted of 150 Gm. of potato and 30 Gm. each of barley, rice, and bread (toast), which contained, respectively, 30.0, 22.4, 22.4, and 15.0 Gm. of carbohydrate. Incidentally, in the 20 diabetic patients studied, the glycemia and glycosuria after the ingestion of 90 Gm. of starch and 100 Gm. of dextrose were identical.

The authors were in error in using 100 Gm. of dextrose and 100 Gm. of starch because, from the standpoint of carbohydrate value, these amounts are not equivalent. The elementary formula for starch is $(C_6H_{10}O_5)_n$ with a molecular weight of n (162). The molecular weight of dextrose $(C_6H_{12}O_6)$ is 180. The complete hydrolysis of 90 Gm. of starch yields 100 Gm. of dextrose.

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To the Editor:—The comments of Dr. Wishnofsky on the article by Dr. Millhon and myself are of interest. This test was originated and standardized by Dr. Althausen and his associates. Their original report excited much enthusiasm for this test as a diagnostic aid in pancreatic disease. Dr. Millhon and I merely published our experience with the test because we were unable to duplicate the results reported by the original authors. We do not claim that this is a satisfactory test of pancreatic function. The basis of the test is that intestinal amylase must be present to break down starch, a polysaccharide, so that it may be absorbed in the form of disaccharides or monosaccharides from the intestinal tract. Therefore, the suggestion of Dr. Wishnofsky that we use well-cooked starch is not valid. Well-cooked starch is already reduced, to a great extent, and therefore would not depend on the presence of amylase for its absorption.

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NEW YORK INDIGENT MEDICAL CARE PROGRAM

To the Editor:—In the interesting department of The Journal, Medicine at Work, Jan. 10, 1959, pages 143-151, the material on nursing homes implied that an indigent medical care program was not available in New York state. New York state has one of the oldest and most adequate systems of medical care for the needy and the medically indigent in the United States. Any person who requires medical care but cannot pay for it may receive that care as a public charge. It is provided through the medical-care services of the local public welfare department and through the hospital-care program of the local community.

The local public welfare program provides medical, surgical, dental, nursing, hospital, laboratory, x-ray, radium, physiotherapy, and allied services, including medicaments and prosthetic appliances, for all persons on the public welfare rolls who require such care and for medically indigent persons as well. There is no limitation as to type, kind, or amount of medical care which an eligible person may receive. It is granted by the local welfare departments as needed, on advice of a physician. It may be provided in a physician's office, the patient's home, a hospital, a nursing home, or in other facilities. Local welfare departments provide these services primarily by purchasing them from local physicians, surgeons, and other medical personnel and from local facilities such as hospitals, dispensaries, specialized medical institutions, and nursing homes.

A monthly average of about 500,000 men, women, and children on the public assistance rolls receive medical care as needed, as do 40,000 children in foster-family homes and child-care institutions and 5,000 aged men and women in public homes. State, local, and federal funds pay for this medical care. In addition, a monthly average of 50,000 medical indigents have their hospital and dispensary bills paid by their local communities. In 1957 about $200,000,000 was spent for the medical care of welfare recipients and the medically indigent by public welfare agencies in New York state.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Testimony by Witnesses of Different Schools of Practice Than That of Defendants.—This was an action for damages for injuries resulting from the alleged negligent conduct of the defendant osteopathic surgeons. From a judgment in the trial court in favor of the plaintiff, the defendants appealed to the court of civil appeals of Texas.

Following the performance of a total hysterectomy by the defendant osteopathic surgeons, the plaintiff failed to void urine for 48 hours. Then she started to urinate uncontrollably through the vagina rather than the urethra. This condition continued after she was dismissed from the defendants' clinic. She eventually went to Baylor Hospital and underwent corrective surgery for the repair of a vesicovaginal fistula, the surgeons being members of the allopathic rather than the osteopathic school of medicine.

It was the contention of the defendants that the plaintiff had not established proof of their negligence by doctors of the same school of medicine as they practiced. The plaintiff's witnesses were the allopathic surgeons who performed the later corrective surgery at Baylor Hospital.

In an earlier decision of the Supreme Court of Texas, the court said, "It is definitely settled with us that a patient has no cause of action against his doctor for malpractice, either in diagnosis or recognized treatment, unless he proves by a doctor of the same school of practice as the defendant (1) that the diagnosis or treatment complained of was such as to constitute negligence, and (2) that it was a proximate cause of the patient's injuries." A limitation of this general rule was stated in a later case, however, to the effect that testimony of physicians of a different school is competent (1) where the subject of inquiry is common to and equally recognized in all fields of practice; or (2) relates to the manner and use of electrical or mechanical appliances commonly used in all fields of practice.

The evidence in this case indicated that the methods, training, and dangers incident to the operation in question are common to both schools of medical practice and equally recognized. The evidence also showed that the acts and omissions proved in the case would amount to negligence in any locality and that no surgeon of any school should leave a patient, after a hysterectomy, with blocked ureters and fistulas in both bladder and vagina.

The judgment in favor of the plaintiff was therefore affirmed. *Miles v. Meadows,* 309 S. W. (2) 284 (Texas, 1958).

MEDICAL FILM REVIEWS

Correction of Micrognathia: 16 mm., color, sound, showing time 12 minutes. Prepared by James W. Kelley, M. D., Tulsa, Okla. Produced in 1958 by Bud Woods Productions, Tulsa. Procurable on loan from James W. Kelley, M.D., 204 Utica Square, Tulsa.

This is a good film on one method of treatment of an infant with severe micrognathia. The approach is fairly new: the tongue is sewn to the lower lip to keep the tongue from falling back during the critical period of early infancy. After a few months the tongue can be freed with no apparent damage. The photography and sound are very good and the techniques used are all clearly illustrated. This film is recommended for oral surgeons, pediatricians, general practitioners, and medical students.

The Larynx and Voice: Physiology of the Larynx Under Daily Stress: 16 mm., color, sound, showing time 23 minutes. Sponsored by the William and Harriet Gould Foundation. Prepared in 1958 by and procurable on rental or purchase ($100) from Hans von Leden, M.D., 30 N. Michigan Ave., Chicago.

This is the second in a series of films on the larynx and voice. It demonstrates the complex pattern of laryngeal function during everyday life and presumes a knowledge of the fundamental anatomy and physiology of the larynx which was described in the first film entitled "Function of the Normal Larynx." This film goes into somewhat more detail. The photographic equipment and technique are shown in greater detail, and many high-speed pictures of the larynx in action have been included. In addition, there is a discussion of the physics of laryngeal activity and how the laryngeal tone may be produced and modified. This film would make a good addition to an undergraduate college course in biology, a graduate course in anatomy and physiology of the vocal mechanism, and anatomy courses given to medical students. There is sufficient detail and information to provoke further interest and to provide the student with a working knowledge of the laryngeal structure.

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

You and Your Eyes: 16 mm., color, sound, showing time 8 minutes. Produced in 1956 by Walt Disney Productions, Burbank, Calif. Procurable on loan (service charge $1.50) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film discusses the eye—how it works and how the function of seeing takes place. Jiminy Cricket introduces the subject by pointing out how highly developed is man's sense of seeing compared to his other senses, and how his inventions of telescope and microscope have extended his capabilities. He also sets down some safety rules for proper care of the eyes. This is an extremely attractive film. It is clever, colorful, and amusing and is well suited for showing to children at the kindergarten and lower elementary grade level.

You Are There: The First Major Use of Penicillin: 16 mm., black and white, sound, showing time 25 minutes. Produced in 1955 for a CBS television program. Procurable on loan (service charge $2.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film pictures the events of one week in 1943 when penicillin, still an unknown quantity in medicine, was being tried on a group of patients with chronically infected wounds sustained in the Pacific theater of World War II. After introductory remarks by Walter Cronkite there is a succession of scenes in the Army hospital where the clinical trial took place, in the laboratories of Fleming and Florey in England, the office of Dr. Chester Keefer in Washington, the laboratory of Jasper Kane at Chas. Pfizer Inc., and finally the hospital once again. The film succeeds in giving an audience some appreciation of the dilemmas of patients, doctors, and manufacturers when confronted with a new pharmaceutical preparation. The film is scientifically accurate. Suspense and interest are sustained throughout. It would be best suited for mature nonprofessional audiences and should also be of interest to medical students.

Hormonal Cyto-Diagnosis: Vaginal Smears: 16 mm., color, sound, showing time 21 minutes. Prepared in 1955 by Prof. André Sicard, Faculty of Medicine, Paris. Sponsored by Ciba Limited, Basel, Switzerland. Procurable on loan (service charge $2.00) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film discusses the value of vaginal smears for studying the ovarian cycle, diagnosing functional disorders therein, and applying appropriate treatment. The technique of cytodiagnosis involved is depicted in detail, and the various elements encountered in vaginal smears are described and interpreted. The film also deals with tubal insufflation, hysterosalpingography, and the early diagnosis of pregnancy. This film contains some magnificent photomicrography, and the color photography is excellent. The entire menstrual cycle is reviewed and the various types of cells normally seen in a vaginal smear are demonstrated. This picture represents a magnificent lesson in human vaginal cytology. It is recommended for physicians, cytologists, and possibly for medical students.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Differing Mechanisms of Action of Mercurials, Carbonic Anhydrase Inhibitors, and Chlorothiazide as Diuretic Agents. R. V. Ford and J. B. Rochelle. J. Lab. & Clin. Med. 53:53-63 (Jan.) 1959 [St. Louis].

The authors studied the effects of 3 diuretic agents, given alone or in various combinations, namely, meralluride (Mercuhydrin) sodium, acetazolamide (Diamox), and chlorothiazide (Diuril), on the excretion of sodium and other electrolytes, such as potassium, chloride, and bicarbonate, in the urine of patients with well-controlled chronic congestive heart failure due to hypertensive cardiovascular disease. Beginning at 7 a. m. and throughout the study, isotonic sodium chloride solution was infused intravenously at a rate of about 650 microequivalents of sodium per minute to prevent depletion of body stores of sodium, which might be reflected in decreased urinary sodium, especially after potent diuretic administration. Contemporary observations of glomerular filtration rate (inulin clearance) and renal plasma flow (*p*-aminohippurate clearance) were made.

The primary action of the diuretic agents studied is the augmentation of the renal excretion of sodium. The results of the study suggested that the mechanisms of action of meralluride sodium and acetazolamide are noncompetitive and different, i. e., different "receptor sites" are acted upon or different renal transport mechanisms for the reabsorption of sodium are inhibited. The mechanism of action of meralluride sodium is competitive with that of chlorothiazide; these 2 agents share a single mechanism of action or receptor site (for transport inhibition), but chlorothiazide can "block" the effect of subsequent doses of meralluride sodium, while meralluride sodium cannot "block" the effect of subsequent doses of chlorothiazide on the excretion of sodium. In a similar way the mechanism of action of acetazolamide is competitive with that of chlorothiazide; these 2 drugs share one mechanism of action or receptor site, and yet chlorothiazide apparently can act through another mechanism which is noncompetitive with acetazolamide.

The third mechanism of action as a diuretic exemplified by chlorothiazide cannot be inhibited by the concurrent administration of meralluride sodium and acetazolamide, i. e., the receptor site (for the inhibition of renal reabsorption of sodium) of chlorothiazide cannot be "saturated" by meralluride sodium or acetazolamide. This additional mechanism of action of chlorothiazide may imply involvement of another enzyme system, or it may imply a greater range of activity of chlorothiazide throughout the nephron. Contemporary observations of renal hemodynamics (glomerular filtration rate and renal plasma flow) did not reveal any significant changes.

Atrial Fibrillation and Its Treatment: Observation of 100 Patients. B. Migheli. Omnia therap. 9:225-267 (April-June) 1958 (In Italian) [Pisa, Italy].

One hundred patients with atrial fibrillation, 54 of whom had previously received digitalis, were placed on quinidine therapy. The mitral valve was affected in 63 patients, and myocardial sclerosis was present in 37. Forty-eight patients had cardiac decompensation. The total dosage of quinidine varied between 3.4 and 22.6 Gm. Patients received 200 mg. of the drug on the first day and 400 mg. on the second day, the dosage being gradually increased each day so that from 200 to 600 mg. was added to that of the preceding day. The daily dosage was divided into several doses, with an interval of at least 3 hours between doses. Sinus rhythm was restored in 78 patients (78%).

Better results were obtained with quinidine in patients (*a*) who had not previously received digitalis, (*b*) who had a defective mitral valve rather than myocardial sclerosis, (*c*) who had cardiac compensation rather than cardiac decompensation, and (*d*) who were in the age brackets from 20 to 40 years and from 61 to 70 rather than in the age brackets from 41 to 60 years and from 71 to 80. There was no apparent difference in therapeutic results between the sexes. Of 32 failures, 2 patients died during the administration of quinidine, although death was apparently unrelated to the therapy; the drug was withdrawn from 20 patients before completing the planned regimen. Toxic reactions, which did not induce discontinuance of the therapy, developed in 9 patients, and embolism was observed in 1. Disturbance of the ventricular neu-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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romuscular conduction mechanism was the main toxic effect which induced withdrawal of quinidine from 13 patients. Since this disorder cannot be detected by ordinary clinical means, one or two daily inspections of cardiograms are recommended. Hypotension, vomiting, nausea, vertigo, atrial murmurs, and diarrhea were noted in 13 patients, which induced withdrawal of the drug from 6. Recurrence of atrial fibrillation during hospitalization was observed in 13 instances (12.8%). Quinidine was an efficacious drug for the management of atrial fibrillation in this series of patients. The initial administration should be complemented by complete bed rest, and the patient should be put on a permanent maintenance therapy afterwards.

Gastroscopy. M. Sundberg. Finska läk.-sällsk. handl. 101:38-47 (no. 1) 1958 (In Swedish) [Helsinki].

Sundberg compares the roentgenologic and gastroscopic findings in 71 patients, in whom the final diagnosis was established at operation or autopsy, and analyzes gastric processes—ulcer, carcinoma, polyposis. The roentgenologic diagnosis was correct in 21 of the 29 cases of ulcer, and the gastroscopic, in 16 cases. The roentgenologic diagnosis was correct in 15 of the 28 cases of carcinoma, and the gastroscopic, in 21. Roentgenologic examination gave correct results in 3 of 5 cases of polyposis, and the gastroscopic diagnosis, in 4 cases. In the 9 additional cases in which operation revealed no pathological process in the stomach, the gastroscopic diagnosis was correct, while the roentgenologic examination gave conclusive results in only 2 cases. Four cases of carcinoma were detected only by gastroscopy, and in 5 additional cases, 2 of carcinoma and 3 of ulcer, gastroscopy confirmed uncertain roentgenologic results. Gastroscopy cannot be a substitute for roentgenologic examination but is a valuable supplementary method.

Familial Hypercholesteremic Xanthomatosis: A Preliminary Report. I. Clinical, Electrocardiographic and Laboratory Considerations. J. L. Guravich. Am. J. Med. 26:8-29 (Jan.) 1959 [New York].

In an attempt to correlate the serum lipid and lipoprotein determinations with the clinical and electrocardiographic findings in 2 families with the hypercholesteremic trait, the author studied 103 persons, 99 of whom belonged to one family (designated kindred 1) and 4 to the other family (designated kindred 2). Thirty-eight persons in kindred 1 and 3 persons in kindred 2 were found to have hypercholesteremia. These included 3 who were spouses. Twenty-five persons had serum cholesterol values in what has been designated a "borderline" zone, i. e., from 250 to 300 mg. per 100 cc. Thirty-seven persons had normal cholesterol concentrations. It is suggested that some of those whose serum cholesterol values were in the "borderline" zone might actually be hypercholesteremic. Some persons were stable and others were labile with respect to their serum cholesterol values. Thus, single estimations are not always to be relied on as a basis for determining normalcy or abnormalcy. In all 41 persons with hypercholesteremia, the S_f 0-12 lipoprotein values were elevated; the S_f 12-20 lipoprotein values were elevated in most of these persons; in slightly more than half of the persons in whom the results of lipoprotein determination were available, there was an elevation of the S_f 20-100 fractions, while the S_f 100-400 lipoprotei values were normal in most instances. The lipoprotein values were normal or near normal in th "borderline" persons and in persons with a norma cholesterol serum level.

Tendon, fascial, or periosteal xanthomas occurre in 23 of the 41 patients with hypercholesteremia They did not occur in any of the spouses. In addition to the commonly described sites of origin some xanthomas were observed originating in site not previously described: the plantar aponeurosis periosteum overlying the lower tibia and media malleoli, and the peroneal and posterior tibia tendons. Cutaneous xanthomas (excluding xanthelasmas) occurred in 2 patients. Xanthelasmas wer observed in 6 patients. Although the incidence o xanthomas increased with increasing age, the relationship was not absolute, some patients wit hypercholesteremia having reached the 6th and 7t decades without the development of xanthomatosi Some correlation between xanthomatosis and th degree of hypercholesteremia was observed, bu here again there were exceptions. No xanthoma were found in persons with normal serum cholesterol levels or in "borderline" persons. Arcus senili occurred in 22 patients with hypercholesteremi 11 of whom were less than 50 years of age. Only persons with normal serum cholesterol levels an 2 "borderline" persons had arcus senilis.

Fourteen patients with hypercholesteremia ha clinical coronary artery disease. Four of these die of coronary occlusion in the course of the author study. All had electrocardiographic abnormalitie either in the electrocardiograms taken at rest o after the two-step test. In 16 asymptomatic patien with hypercholesteremia, the Master two-step te was carried out; the response to exercise was abnormal in 9. It is suggested that, in some of thes patients, this test might indicate "occult" or presymptomatic coronary artery disease. Anginal pai was not present in the "borderline" group, but ther was electrocardiographic evidence of an old posterior infarct in one patient. Of 16 two-step test 5 were positive. In the group of persons with no mal serum cholesterol levels, one patient had def nite clinical coronary artery disease (an ol posterior infarct), and 2 were suspected of havin angina pectoris. One of the latter had a positiv two-step test. Two of 10 asymptomatic patien with normal serum cholesterol level who underwent this procedure had positive two-step tests. The incidence of hypertension and cerebrovascular and peripheral vascular disease in this series was low. It is suggested that hypertension and diabetes are more likely to be associated with these forms of atheromatous disease than is hypercholesteremia per se. Age too is an important factor; all but one of the patients who had clinical evidence of aortic or peripheral arterial disease or who showed calcification of pelvic or lower limb arteries on x-ray examination were in the 6th or the 7th decade. These data again point up the pathogenetic relationships between hyperlipidemia and the clinical manifestations of xanthomatosis and atherosclerosis. Taking into account the factors of age and sex, there was a general, although by no means absolute, correlation between blood lipid levels and the development of xanthomas and coronary artery disease, overt or subclinical.

The Incidence of Gall Stones. J. R. Cain and H. Donato. J. South Carolina M. A. 55:17-19 (Jan.) 1959 [Florence].

The authors investigated the relative incidence of gallstones with regard to sex, age, and race. Their report is based on 6,107 autopsies performed at the Medical College of South Carolina and the Roper Hospital in Charleston during 1913-1948. In order to ascertain whether improvement in diet might be accompanied by an increase in the incidence of gallstones, the autopsy records were divided into 2 groups, depending on whether the autopsies were performed before or after 1939. It was felt that the increased incidence should be more apparent in the Negro race, since Negroes had probably made proportionately greater strides in recent years in enhancing their diet.

The authors found that the white race is approximately 3 times more susceptible to gallstones than the Negro race. Equally striking is the consistent sex difference, with females having a significantly higher incidence than males and with white females having the highest incidence. The incidence of gallstones rises with age; they are rare in children. Whether the slight increase in incidence of gallstones during 1940-1948, over 1913-1939, is significant cannot be determined.

Studies of the Influence of Comfortable and Hot and Humid Environments Upon the Rate of Excretion of H^3, H_2O, Cl^{36}, Cl^{35}, Na^{23}, Rb^{86}, and K^{39} in Control Subjects and Patients with Congestive Heart Failure. G. E. Burch and C. T. Ray. J. Lab. & Clin. Med. 53:89-105 (Jan.) 1959 [St. Louis].

The authors studied the influence of a hot and humid hospital environment during the summer on certain phases of electrolyte and water metabolism in 9 women, between the ages of 22 and 65 years; 5 of these patients had chronic congestive heart failure, and the other 4 (1 convalescent from a respiratory infection, 1 with tuberculous arthritis, 1 with sarcoidosis, and 1 convalescent from a lung abscess) served for contratests. These 9 patients were studied in 2 wards of the Charity Hospital of Louisiana in New Orleans; one ward was air-conditioned, and the environment of the other ward was hot and humid. The patients spent about equal time (2 weeks) in both environments. Three of the patients with chronic congestive heart failure and 2 of the contratest patients were given intravenously radiochloride (Cl^{36}), radiorubidium (Rb^{86}), and tritium hydroxide (H^3OH) simultaneously at the onset of the studies. Dietary intake of sodium, chloride, potassium, and water was recorded, and the urinary excretion of these substances was measured. Urinary clearance rates were determined for Cl^{36} and Rb^{86} as well as stable chloride, stable sodium, stable potassium, and tritium (radiohydrogen, H^3). Osmolar excretion, glomerular filtration rate, and renal tubular reabsorption were measured.

The results showed that a hot and humid summer environment produced in most of the patients a significant increase in extrarenal losses of water and electrolytes, even though the patients were at bed rest. In addition, there was an increase in osmolarity of the urine, with a tendency to negative-free water clearance. An unusual voluntary intake of water developed in some of the patients acclimatized to a hot and humid summer and continued while they were in the air-conditioned ward where extra requirements for water were not necessary. The habit of drinking large quantities of water appeared to be a manifestation of acclimatizing adjustments made by some people of Louisiana to the heat and humidity of summer. Probably with a longer period of residence in the cool environment the intake would have declined to the usual levels. The high intake, although adequate for the hot and humid environment and assuring essentially an average normal urinary state, resulted in a diluted urine of large volume when continued in the cool environment.

The experiments revealed marked daily fluctuations in urinary clearance and excretion of Cl^{36}, Rb^{86}, stable chloride, stable sodium, stable potassium, tritium, and water, when intake of these substances and physical activities were relatively constant. In view of these variations it is necessary to exercise caution when observing renal function and urinary excretion with only a few such measurements. The daily endogenous creatinine clearances recorded for 26 consecutive days revealed no significant differences between time course and magnitude of rate of glomerular creatinine clearance of the patients with or without chronic congestive heart failure. The patients with heart failure had both remission and exacerbations in their failure during the observation period. It was evident that any variations in renal function associated with the congestive heart failure were primarily tubular. It would likewise appear that, unless congestive failure is severe, glomerular filtration remains within normal limits, at least for patients with moderately severe chronic congestive heart failure.

Although only 3 radioactive isotopes were employed in this study, it revealed the facility with which renal function may be followed continuously and simultaneously with different radioactive isotopes. A larger number of such isotopes could be used equally well by taking advantage of differences in rates of physical decay and energy and spectrums of radiation. By adding support to the physiological data previously described in man, with and without chronic heart failure, for Cl^{36}, Rb^{86}, stable chloride, stable sodium, and stable potassium and by adding the simultaneously observed renal excretion of H^3OH, the authors' study increased the validity of the findings for man as a whole.

Primary Diffuse Interstitial Pulmonary Fibrosis (Hamman-Rich) Syndrome. E. Hansen. Nord. med. 60:1710-1715 (Nov. 27) 1958 (In Danish) [Stockholm].

The Hamman-Rich syndrome is a diffuse, progressive, interstitial fibrosis of the lungs of unknown etiology, ending in death after a few years and in especially fulminant cases within a few months. The pathological picture presents characteristic and marked changes. In clinically and roentgenologically suspected cases, diagnosis can be decided only by taking a lung specimen for biopsy. Hamman and Rich emphasize that the syndrome is distinguished from the carnification process after an unresorbed croupous pneumonia in that there is only a slight tendency to organization of the intra-alveolar exudate and that the growth of connective tissue into the alveoli seen in carnification is lacking. The main symptoms are cough, with as a rule no, or only scanty, viscous expectorate, dyspnea that develops gradually, and increasing cyanosis. The roentgenologic findings, as a rule, leave no doubt as to a pulmonary disease but are so atypical that the diagnostic possibilities are numerous. The disease is primary in the sense that it cannot be ascribed to any preceding pulmonary disease, but a relation to earlier virus pneumonias cannot be excluded. Recent experiences seem to show that steroid treatment can at least temporarily stop or retard the fibrosing, but renewed progression after ended treatment indicates that the unknown stimulus continues to be active and the effect of the steroid treatment is only a suppression of the organism's reaction to this stimulus. The latest report on the effect of cortisone treatment over a longer period apparently permits a certain therapeutic optimism. The effects of corticotropin and cortisone make these drugs useful in the treatment of relatively new and rapidly progressive cases and improve the hitherto bad prognosis.

Agammaglobulinemia and Respiratory Infection. J. Bouton, E. Fogel Korc, I. Korc and others. Tórax 7:89-118 (June) 1958 (In Spanish) [Montevideo, Uruguay].

A deficiency or absence of gamma globulin in the blood, either idiopathic or occurring secondarily to diseases of the lymph nodes or of the reticuloendothelial system, is rare. The main features characterizing agammaglobulinemia are: (1) multiple infections, especially respiratory infection; (2) absence of antibodies and isoagglutinins; and (3) absence of serum gamma globulin in the electrophoretic proteinogram, whereas the other fractions are normal. The condition may be treated by the periodic administration of intramuscular injections of purified gamma globulin (human) so as to prevent recurrences of the infections. Respiratory infection, as a rule, occurs in association with gastrointestinal and other infections and is often complicated by fatal suppurative meningitis. There is neither acquired nor induced immunity, as evidenced by a negative tuberculin reaction and by positive Dick and Schick reactions. Sputum cultures during bouts of respiratory infection have revealed Diplococcus pneumoniae as the predominant organism. Both in the acute and in the chronic phases of the disease, the sputum is negative for tubercle bacilli.

The authors report the case of a 17-year-old girl, who was hospitalized in the Pablo Purriel Hospital of Montevideo during an episode of respiratory infection, from which she had suffered since the age of 3 years. Bilateral bronchiectasis had been observed at the age of 6, and splenomegaly and symptoms of hypersplenism at the age of 10. These symptoms paralleled the recurrent respiratory infection and regressed with remission of the disease. A brother who had also suffered from recurrent respiratory disease since birth died at the age of 10 months of bronchopneumonia complicated by meningitis. The electrophoretic proteinograms of the parents and of 3 sisters were normal, but those of 2 brothers showed hypogammaglobulinemia. The grandparents of all these siblings were first cousins. The patient, on hospitalization, had anemia as well as agammaglobulinemia, and a sternal myelogram showed changes of granulocytic hyperplasia. Treatment consisted of the intramuscular injection of a 12% solution of purified gamma globulin (human) in a dosage of 0.15 cc. per kilogram of body weight. Tetracycline and nystatin were also given but only during the period of acute infection. Gamma globulin continued to be administered in individual doses and at intervals which were adjusted according to the ratio of serum gamma globulin in the periodically controlled proteinograms. With this maintenance therapy the patient's bronchopulmonary symptoms and diarrhea subsided, splenomegaly was greatly diminished, anemia disappeared, and leukocytosis became normal. The respiratory and other infections have not recurred, and the ratio of serum gamma globulin in the proteinogram stands at 11%.

According to the authors, antibiotics should be administered to patients with agammaglobulinemia only during the period of acute infection. Prolonged or untimely administration may cause resistance of the intestinal bacteria, with consequent chronic intestinal infection. Blood transfusion and the administration of hormones and vaccines, including BCG, are interdicted. Blood transfusion may be followed by a fatal viral hepatitis, and hormones and vaccines are unnecessary, and even dangerous, because of the immunological defects of the patients.

Palpability of the Liver Edge in Healthy Adults. E. D. Palmer. U. S. Armed Forces M. J. 9:1685-1690 (Dec.) 1958 [Washington, D. C.].

Uncertainty over just how far below the costal margin the right lobe of the adult liver may normally extend seems to be common. The location of the lower edge of the liver does not necessarily bear a relationship to the size of the organ, and one must determine the position of the liver's cephalad limit by percussion before hepatomegaly can be diagnosed. Nevertheless, diffuse hepatomegaly manifests itself almost wholly in the downward direction. Conversely, any great degree of extension of the liver's edge below the costal margin almost always indicates hepatomegaly. The studies described were concerned with the range of positions occupied by the inferior border of the liver's right lobe, as judged by palpation, in a group of normal adults. Observations on the liver were recorded during routine physical examinations on 1,000 military subjects who were free from liver disease.

The author shows that it is necessary to be very precise about the point at which the measurement is made when recording liver size on the basis of the position of its edge. The best point for the determination lies along a line just lateral to the right rectus muscle margin, in the linea semilunaris. The liver edge in 42.6% of the subjects could not be palpated, and in 14.4% it could be felt to descend to the costal margin but not beyond; in 15% it descended 1 cm. below the costal margin; in 12.9% it descended 2 cm.; in 8.2%, 3 cm.; in 5.7%, 4 cm.; and in 1.2%, 5 cm. No correlations could be found between the position of the liver's edge and the subjects' sex, age, height, weight, or subcostal configuation. In commenting on these findings, the author points out that the examinations were made at various times throughout the day. The normal adult liver, which weighs about 1,500 Gm., contains about 800 ml. of blood. The blood content, therefore, exerts an important influence over liver weight and size. Because, presumably, this blood fluctuates with the phase of digestion and physical activity, it must be supposed that liver size may vary significantly from hour to hour during the day and perhaps from day to day.

Experiences with the Artificial Kidney at the Medical College Hospital. C. M. Smythe, A. V. Williams and J. Buse. J. South Carolina M. A. 55:5-9 (Jan.) 1959 [Florence].

The authors summarize experience gained with extracorporeal dialysis in the treatment of patients with acute renal failure at the Medical College Hospital in Charleston. They used the Kolff type of disposable dialyzing unit for 16 dialyzation treatments in 11 patients chosen from a large group with acute and chronic renal failure. On the basis of a detailed case report, the authors show that during the development of hyperkalemia or uremia dialysis will have to be repeated at frequent intervals. In general, timing of dialysis and careful attention to fluid and electrolyte balances and to electrocardiographic changes proved important.

Diagnosis has remained a major problem. Not only has it been difficult to judge the exact etiological agent causing acute anuria but even whether a patient has acute renal disease. Acute renal failure after acute trauma is simple enough to diagnose. However, in postpartum patients the differential diagnosis between tubular and glomerular injury may be difficult. This is of vital importance, for severe glomerular destruction is essentially irreversible. Difficulties arise also in patients with medical problems. Thorough history taking is important to establish the presence or absence of preexisting renal disease. Eyeground changes, heart size, cardiac contour, and electrocardiographic changes may help in differentiating an exacerbation of chronic renal disease from acute renal disease.

The authors found the dialyzing apparatus to be serviceable and practical. Six of the 11 patients survived. Four of these had acute renal failure, and all 4 are well at present. Three of the 5 patients who died were examined at autopsy and were found to have irreversible kidney disease.

Corticotrophin and Steroids in the Diagnosis and Management of "Obstructive" Jaundice. W. H. J. Summerskill and F. A. Jones. Brit. M. J. 2:1499-1502 (Dec. 20) 1958 [London].

In 12 patients with obstructive jaundice of uncertain cause, the effect of a 5-day trial of steroid or corticotropin therapy was of great value in reducing serum bilirubin levels and in differentiating between intrahepatic obstruction due to hepatitis and extrahepatic obstruction. Serum alkaline phosphatase concentrations also fell during treatment, although to a less extent, thus suggesting that the reduction of jaundice caused by corticotropin or steroid drugs was due to increased bile excretion. The drugs acted immediately, and no difference was apparent between corticotropin and steroids.

These findings accord with earlier observations that corticotropin and steroid compounds may influence the jaundice both of hepatitis and of extrahepatic obstruction, but they challenge the conclusion that the drugs have no value in the differential diagnosis between the 2 conditions. Four of 5 patients with intrahepatic obstructive jaundice due to hepatitis had reductions in serum bilirubin levels which exceeded any that occurred in patients with extrahepatic obstruction due to tumor. The "critical" figure in this series was a fall in the serum bilirubin level of 8% or more a day in a period of 4 to 8 days, and review of earlier studies in patients with extrahepatic biliary obstruction shows that such a response to corticotropin is rare. The continued administration of the drugs to those who have shown a response to the initial test permits a confident diagnosis of hepatitis, if there is sustained improvement. Corticotropin or steroid therapy is the treatment of choice for such patients. Failure to improve with treatment does not exclude hepatitis. In viral hepatitis, a proportion of patients may present with variable clinical, biochemical, or histological features of obstruction. Six patients with such cholangiolitic findings responded to corticotropin much better than many other patients with hepatitis.

SURGERY

Spontaneous Hematoma of the Rectal Abdominal Muscles: A Clinical Contribution. A. Pannella. Riforma med. 72:1303-1308 (Nov. 15) 1958 (In Italian) [Naples].

Three patients, 2 female and 1 male, aged 70, 78, and 74 years, respectively, with spontaneous hematoma of the rectal abdominal muscles are reported on. The symptoms appeared suddenly in all the patients, the condition having been caused by spells of coughing. Swelling occurred on the left side of the epigastric region in one patient and to the right of the mesogastric region in the other two. The surface of the swelling was smooth in the first and second patients, the skin covering the swelling having an ecchymotic color in the first patient and a color which was between dark blue and yellowish green in the second. There was also an ecchymotic discoloration of the skin swelling in the third patient. In all the patients this swelling, after having appeared suddenly, regressed gradually within a short period of time. No intestinal disturbances or peritoneal symptoms were present, but all the patients had arteriosclerosis. The first and third pa tients were subjected to medical therapy and the second to surgical therapy, with good results.

On Surgically Treated Herniated Intervertebra Discs. B. Knutson and G. Wiberg. Acta orthop scandinav. 28:108-123 (no. 2) 1958 (In English [Copenhagen].

The authors report on 134 men and 117 womer between the ages of 16 and 68 years, who wer operated on for protruded or herniated interverte bral disk in the department of othopedic surger of the University Hospital of Lund, Sweden. Weak ness in dorsal flexion of the great toe was noted i 58 (71%) of 82 patients, in whom the power of thi dorsal flexion was tested and in whom surgic intervention revealed protrusion or prolapse of th disk at the 4th and 5th lumbar vertebrae levels. C those patients on whom paresis of the great toe wa observed, surgical intervention revealed protrusio or prolapse of the disk between the 4th and 5t lumbar vertebrae in 63%. Of the 133 patients i whom surgical intervention revealed prolapse the disk between the 5th lumbar and 1st sacr vertebrae, the achilles tendon reflex was impaire or absent in 111 (83%). Of those patients in whor clinical examination revealed impairment or al sence of the achilles tendon reflex, surgical inte vention revealed protrusion or prolapse of the dis between the 5th lumbar and 1st sacral vertebra in 81%.

Myelography was performed with the aid of ai oxygen in 80 patients and with the aid of a wate soluble Scandinavian contrast medium preparatio in 63 patients. Of those in whom myelograph showed a protrusion between the 4th and 5th lun bar vertebrae, surgical intervention confirmed tl finding in 77% of those from whom myelogran were obtained with air-oxygen, and in 93% of tho from whom myelograms were obtained with tl aid of the contrast medium. Surgical interventic revealed protrusion or prolapse of the disk betwee the 4th and 5th lumbar vertebrae in 36% and pr trusion or prolapse of the disk between the 5 lumbar and 1st sacral vertebrae in 69% of tho patients in whom myelography with air–oxyge had shown no signs of an abnormal condition. Su gical intervention revealed protrusion or prolap of the disk between the 4th and 5th lumbar vert brae in 1 patient, and between the 5th lumbar an 1st sacral vertebrae in 9 of 12 patients whose myel grams obtained with the aid of the contrast mediu did not show any signs of an abnormal conditio Myelography with the aid of a water-soluble co trast medium gives more reliable results than my lography with the aid of air–oxygen, but a certa degree of roentgenologic overdiagnosis and unde diagnosis must be expected.

A questionnaire was mailed to the 251 patients within 4 to 12 years after the surgical intervention, and 241 (96%) replied. Improvement was reported by 228 (94.5%), and the remaining 13 patients (5.5%) reported no change or deterioration. The time required for postoperative recovery varied from 6 weeks to 1 year.

Surgical Treatment of Stenosis of the Aqueduct of Sylvius: Considerations on 75 Patients Operated On. I. Papo and R. Tritapepe. Minerva chir. 13: 1299-1305 (Nov. 30) 1958 (In Italian) [Turin, Italy].

The authors report on 75 patients with hydrocephalus caused by stenosis of the aqueduct of Sylvius, who were operated on during the period from 1938 to 1957 in the surgery clinic of the University of Milan. Sixty-two patients were below 30 years of age. One of 2 patients subjected to decompression of the posterior cerebral fossa was dismissed from the hospital in fair condition but was lost sight of; the other patient was still alive and working 13 years after the operation. One patient subjected to removal of the obstruction died of purulent meningitis.

Twelve of the 62 patients subjected to ventriculocisternostomy, according to the Stookey-Scarff technique, died while still in the hospital. Ten of these patients derived no benefit from the operation and showed no improvement. Immediate onset of increasing coma followed in 8 patients who later suffered marked hyperthermia and decerebrate rigidity. One patient during the operation, carried out under local anesthesia, suffered general epilepsy with cerebral edema, which caused death after a few hours. One patient soon after the operation developed intense bronchorrhea, with respiratory disturbance and cardiocirculatory insufficiency, and died 5 days later. Two patients who died in hyperthermic coma, with severe cerebrospinal hypertension, at preoperative cisternography presented a blocking at the level of the cisternae basales. Two patients, after deriving some benefit from the operation for a period of 9 and 5 days, respectively, suffered a relapse of the intracranial hypertension, which became progressively worse and was accompanied by sopor; hyperthermic coma and decerebrate rigidity developed later. These patients died 12 and 30 days, respectively, after the operation.

The Stookey-Scarff ventriculocisternostomy was not sufficient in 12 patients to check permanently the intracranial hypertension. Seven of these patients eventually were subjected to other procedures. Of the 5 patients who were not reoperated on, 2 showed postmeningeal blocking, with obstruction of the cisternae basales, and derived no benefit from the operation; one of them died after 2 months. A third patient showed no clear remission of the symptoms of hypertension and was readmitted to the hospital after 7 years, with dementia, severe reduction of vision, and astasia-abasia. In the remaining 2 patients relapse of hypertension occurred a few months after the operation, and one of them died within 4 months. Ventriculocisternostomy according to the Stookey-Scarff technique, however, had a beneficial effect on 34 patients, in whom a good equilibrium was obtained, and the intracranial hypertension disappeared. Twelve of these patients were lost sight of, but 22 are still alive and in good condition from 14 months to 15 years after the operation.

Some patients who derived no benefit from the Stookey-Scarff operation were later subjected to the Torkildsen operation but with no success. In addition, the Torkildsen ventriculocisternostomy was performed, as the first operation, on 8 patients. The first patient died on the second day in hyperthermic coma after exploration of the posterior cerebral fossa. The second patient died of purulent meningitis a few weeks after the operation, and the third patient died after 40 days. The fourth patient, who most likely had a neoplasia of the cerebral trunk, died 19 months after the operation. The fifth patient, who had been dismissed from the hospital after a normal postoperative course and disappearance of the hypertensive syndrome, was lost sight of. The remaining 3 patients were found to be in good condition 28, 27, and 12 months, respectively, after the Torkildsen operation.

A Statistical Comparison Between the Future Condition of Patients with Mitral Valve Disease Operated On and of Those Not Operated On. E. Donzelot, R. Heim de Balsac, P. Samuel, and E. Beyda. Semaine hôp. Paris 34:2855-2858 (Nov. 28) 1958 (In French) [Paris].

The authors report on 322 patients with disease of the mitral valve, who were examined or operated on between February, 1951, and September, 1954, and whose conditions were followed for from 20 months to 5 years. One hundred sixty-five patients were operated on, and 157 were not. Those who did not undergo surgery were assigned to 4 categories. In the first category were 120 patients who were not in operable condition because of large valvular lesions, hypertension, or nonreducible cardiac insufficiency. Although 59 of these patients died, 61 are still living but have had to limit their activities. The 7 patients in the second category included those with such temporary contraindications to operation as progressive renal tuberculosis, pulmonary tuberculosis, bacterial endocarditis, and bouts of rheumatism. Three of these patients later underwent commissurotomy, 3 others soon will, and the 7th patient is still in inoperable condition. The 11 patients in the third category were classified as having a mitral stenosis which was not serious enough to warrant operation. [The cross-sectional area of the mitral aperture must be not less than 2 sq. cm. if it is to permit sufficient flow of blood; patients with stabilized mitral valve disease are much more numerous than the statistics show, because many of them do not consult a physician.]

The fourth category consisted of 19 patients whose mitral stenosis indisputably indicated a commissurotomy but who were not operated on. In this group 12 refused intervention, 6 agreed to it but postponed the operation, and 1 died before he could be prepared for surgery. All 19 patients in category 4 were considered candidates for operation in accordance with the same criteria which were applied to the 165 patients who underwent surgery. All conditions of age, sex, clinical state, etc. were analogous. The authors have made a valuable comparison between the outcomes in the 19 patients who refused operation and the 165 patients who agreed to it; there were 16 deaths among the latter (or a mortality rate of 9.7%) and 11 deaths among the former (or a mortality rate of 58%). The conditions of 2 patients among the 165 and of 4 among the 19 grew worse. But of the 165 patients who underwent surgery, the conditions of 133 (or 80%) improved, 100 to the point where they could return to work and could lead a normal life.

The gravity of spontaneous evolution of mitral stenosis in its pure form, or in forms associated with a mitral insufficiency or another lesion, is evident from the fact that 50% or more of these patients die within 5 years if there is no intervention. The change brought about by commissurotomy shows the great value of this intervention.

Possibilities and Limitations of Induced Hypothermia in Operation on the Bloodless Heart: Experimental Study. A. Martelli, E. Belelli and L. Urso. Clinica 18:301-316 (no. 5) 1958 (In Italian) [Bologna, Italy].

Direct intracardiac surgery by induction of hypothermia was experimentally studied in 20 dogs, divided into 5 groups. All the dogs were immersed in an iced bath until the rectal temperature reached 30 C (86 F). Then the chest was opened through the 4th right intercostal space; this procedure was followed by arrest of circulation, incision and closure by suture of the right atrium, and rewarming to normal body temperature. Of 4 dogs in the first group, arrest of circulation lasted between 5 and 15 minutes in 2 dogs. Sinus rhythm was restored in one dog, and defibrillation through massage and electric shock was required in the other dog. Irreversible fibrillation took place in the remaining 2 dogs, in which circulatory arrest lasted longer than in the first 2.

Cannulation through the subclavian or the right carotid artery and injection of oxygenized blood into the coronary arteries were added to the preceding procedure in the second group of 4 dogs. Irreversible and fatal ventricular fibrillation developed in all 4 dogs. Arrest of circulation was preceded by injection of procaine hydrochloride into the node of Keith and Flack in the third group of 3 dogs. This method was useful in preventing fibrillation, and sinus rhythm was restored in all 3 dogs. Cardiac and circulatory arrests were induced by the administration of potassium citrate in heparinized blood according to the technique of Melrose in the fourth group of 4 dogs and by administration of acetylcholine according to the technique of Moulder in the fifth group of 5 dogs. Ventricular fibrillation, which was mostly irreversible, took place in the dogs which received potassium citrate. No ventricular fibrillation was observed in the dogs which received acetylcholine. The authors conclude that hypothermia has limited application in surgery despite the use of drugs for prevention of ventricular fibrillation.

The Treatment of Papillary Carcinoma of the Thyroid Gland. O. H. Beahrs and L. B. Woolner. Surg. Gynec. & Obst. 108:43-48 (Jan.) 1959 [Chicago].

Views on methods of management of carcinoma of the thyroid vary widely. Some physicians are of the opinion that certain malignant lesions should not be treated surgically at all; some advise only conservative surgical measures, while others recommend radical surgery. In general, carcinomas of this gland can be divided into 2 groups: (1) those of low degree of malignancy, the majority of which are papillary carcinomas, and (2) those of high degree of malignancy, the anaplastic carcinomas. The behavior pattern of each group is decidedly different from that of the other. As currently defined, in the section of surgical pathology at the Mayo Clinic, papillary carcinoma is a well-differentiated tumor which usually shows a striking mixture of papillary and follicular structural components. Within the papillary group there is considerable variation in size of the primary lesion and the degree of invasiveness of the tumor. Certain papillary carcinomas may be minute, even microscopic, and yet be associated with bulky nodal metastasis.

This study was undertaken to evaluate a series of patients with papillary lesions, who had been included in a 1951 report from the Mayo Clinic concerned with patients who had been treated for carcinoma of the thyroid between 1938 and 1947 inclusive. The records of the 174 in whom the lesions were previously classified as papillary carcinoma were restudied. Twenty-four patients were excluded, the lesions in most of them being angioinvasive follicular and solid carcinomas or papillary adenomas. In 136 of the remaining 150 cases, definitive surgical treatment was carried out. Thirteen patients had inoperable lesions, and biopsy only was performed. One patient had palliative lobectomy; at the time of operation gross carcinoma remained in the midline portion of the neck. The treatment and survival rates for the 136 patients who received what was thought by the surgeon to be curative surgical treatment have now been evaluated.

Lobectomy on the side of the lesions or subtotal thyroidectomy was performed on all the patients except 2 on whom total thyroidectomy was done. Metastasis to cervical nodes occurred in 47.1%. The patients were treated by modified neck dissection, except in 5 instances in which radical neck dissection was carried out. No cervical procedure was done for patients who did not have clinically involved cervical nodes or for those in whom nodes could not be felt at the time of operation. The 5-year survival rate was 97%; the 10-year rate, 87.9%; and the 15-year rate, 75.5%. These results support the belief that radical operation is not always essential in the management of papillary carcinoma of the thyroid and that neck dissection is not indicated in the absence of known enlarged cervical nodes.

A Report on Studies of Spinal Traction. G. A. Lawson and C. M. Godfrey. M. Serv. J. Canada 14:762-771 (Dec.) 1958 [Ottawa].

Four factors have been suggested as contributing to the effect of traction on painful back and neck conditions: (1) immobilization, (2) reduction of muscle spasms, (3) reorganization of disk material, and (4) vertebral realignment. In commenting on these factors, the authors say, with regard to immobilization, that many backaches get better if the patient goes to bed for 3 weeks. With regard to release of muscle spasm, it has been observed that stretching a painfully tight muscle gives relief from pain. Some investigators have shown by diskogram studies that there is some sucking back of extruded nuclear material into the center of the disk on traction. Regarding separation of the vertebrae, there has been considerable conjecture. The authors cite figures on the range of weights applied and on the duration of traction applied to different parts of the spinal cord. They examined with the aid of x-rays a group of patients before and during cervical or lumbar traction. The films were read without any knowledge of the order in which they had been taken. The roentgenologist attempted to measure the amount of vertebral separation on each film. The reports were appended to the x-ray films and only then was the roentgenologist told which films were taken before and which during traction.

For cervical traction, the authors used an overhead suspension with a bar and a head sling. The patient was seated with his back to the suspension apparatus, and traction was applied by means of a spring-lift scale to the amount and time decided upon. Usually 40 to 60 lb. of traction for 20 minutes was given, a film was taken, and then in some cases 100 lb. was applied for 1 minute with a follow-up film. In 2 patients films were taken before and during horizontal traction. All patients had received traction previously and were relaxed during investigation. For lumbar traction, a canvas hammock-type of traction frame was used. Not only were roentgenologic control films taken, but the height of the patient before and after cervical traction was ascertained. Height measurements were made on 36 patients, who received at least 10 traction treatments, and roentgenologic studies were made on 26 patients. It was found that spinal traction with weights up to 100 lb. on the cervical area and 150 lb. on the lumbar region for varying amounts of time resulted in no significant separation of the vertebrae. Cervical traction resulted in a slight temporary increase in height.

Spontaneous Perforation of the Common Bile Duct: Report of a Case. T. C. Gertz. A. M. A. Arch. Surg. 78:7-11 (Jan.) 1959 [Chicago].

The author reports on a 4½-month-old female infant who had had jaundice of varying intensity since she was 5 weeks old. The stools were acholic, and the urine contained only traces of bile pigments. The abdomen was distended with ascites. The patient had large bilateral inguinal hernias containing fluid. The abdomen was opened through a transverse incision in the epigastrium. On opening, large amounts of bile-stained fluid escaped. The stomach and the duodenum were adherent to the lower surface of the liver and obscured the porta hepatis and the ligament. They were dissected free in order to gain access to the hepatoduodenal ligament. In this procedure a large cavity was entered, the walls of which consisted of heavily bile-stained fibrous and fibrinous tissue. The cavity contained traces of clear bile. Through a puncture of the gallbladder, the gallbladder and the bile ducts were filled with iodopyracet (Diodone), and a cholecystocholangiogram was taken which showed an evident leakage in the inferior part of the common bile duct and an obstruction of the passage to the duodenum. It was not possible to localize the perforation. A rubber tube was placed in the region of the common duct, and the abdomen was closed in layers. Postoperatively, there was profuse drainage of bile for some days, but after 9 days this gradually ceased and the drain was removed. A month after the surgical intervention, the patient was discharged in excellent condition. The inguinal hernias disappeared spontaneously after the operation.

Ten additional cases of spontaneous perforation of the common bile duct in infants between the ages of 3 weeks and 22 months were collected from the literature. The findings in these patients and in the author's patient showed that spontaneous perforation of the common bile duct is a disease typically characterized by a mild, intermittent jaundice, acholic stools, absence of bile pigments in the urine, distended abdomen with ascites, and, very often, bilateral inguinal hernias with fluid. Although the disease may run acutely, the course is mostly subacute. If the disease is let alone, it is occasionally fatal; usually, though, it responds well to surgical intervention, which ought to be performed as soon as the diagnosis has been made. Simple drainage of the region of the common duct has in most patients been adequate. Operative cholecystocholangiography is a valuable diagnostic method.

Prevention and Treatment of Infections in Bone. J. H. Moe. Journal-Lancet 79:2-7 (Jan.) 1959 [Minneapolis].

The author reports the case of a 48-year-old woman with a comminuted fracture of the right lower femur for which she was treated by open reduction and internal fixation with a nail and plate combination. Wound infection occurred despite administration of large daily doses of antibiotics. The operative wound was opened, and evidence of purulent osteomyelitis was found. Amputation through the middle of the thigh was advised but refused by the patient. For one year numerous attempts were made to control the infection without amputation. Rush pins were inserted 10 days after the initial débridement and removal of plate and screws. The wound did not become clear. A high thigh amputation performed with the consent of the patient proved inadequate, and a disarticulation of the hip finally became necessary to control the infection. Plate-and-screw fixation does not serve as a satisfactory method of fixation in the presence of osteomyelitis. The screws loosen, the drill holes become filled with granulation tissue, and the bone becomes necrotic under the plate. A second case of a comminuted fracture of the femur in a 32-year-old man is reported, with satisfactory outcome of a severe infection of the operative wound. The infection had occurred after open reduction with double-plate fixation without external support, requiring 4½ hours because of an inadequate armamentarium of equipment. Plate-and-screw fixation was removed when the wound was opened and débrided. All dead tissue and some bone were removed. This procedure was followed by packing the wound and irrigating it while maintaining position of the fracture by traction in suspension. After one week an intramedullary nail was inserted, and open packing and irrigation with sodium chloride solution and antibiotics were continued for an additional week. Specific antibiotics were given systematically. Subsequently, secondary closure was successful in obtaining soft tissue coverage, with minimal drainage from a small sequestrum visible 2 months later. The wound healed after sequestrectomy.

Excessive operating time in surgical open reduction of fractures invites infection. The use of plates and screws without external fixation provides inadequate internal fixation in comminuted fractures of long bones. Wound infections in open fracture surgery should not be treated expectantly. The surgical principles of complete exposure of the infected area, eradication of the grossly necrotic tissue, removal of all plates and screws, and open packing of the wound for easy dependent drainage are sound. Maintaining position of the fracture fragments and instituting specific antibiotic medication, both locally and systemically, are also of importance. The optimum time for secondary closure is about 5 to 10 days. When secondary closure is done, the wound must be completely obliterated of dead space. Intramedullary nail fixation can be instituted in the presence of infection without hazard. On the other hand, plates and screws are not well tolerated. When bone sequestrates, the necrotic portion must be removed.

The prevention of infection in compound fracture wounds is directly related to the initial care given the wound. Only wounds which are very fresh and thoroughly cleansed should be closed primarily, and such closure must be done without tension. All wounds several hours old and those which are doubtfully clean should be packed open with fine mesh gauze and closed secondarily. External support to the fracture by cast or suspended splinting should always be given. The prevention and control of infections in bone as well as in soft tissue in hospitalized patients require constant vigilance and good surgical judgment. Team work on the part of physicians, nurses, and personnel is of utmost importance. The salient features of a program directed toward eradicating infections are outlined.

The Removal of Excessive Potassium and Ammonium from Bank Blood Prior to Transfusion. D. C. Schechter, T. F. Nealon Jr. and J. H. Gibbon Jr. Surg. Gynec. & Obst. 108:1-6 (Jan.) 1959 [Chicago].

Blood undergoes certain biochemical changes during storage, the most significant of which, for the recipient of the blood, are the greatly increased concentrations of ammonium and potassium. The authors investigated this increase and describe a simple method for removing excessive potassium and ammonium from stored blood prior to transfusion. They collected from the cubital vein of each of 27 male volunteers 500 ml. of whole blood. A sample was withdrawn for chemical analysis, and the remainder of the blood was stored at 5 C. The blood from 9 of these men (group A) was collected in 500-ml. silicon-coated vacuum bottles (Transfuso

Vac), containing 120 ml. of acid-citrate-dextrose solution, U.S.P. formula B. Three bottles were stored for 7 days, 3 for 14 days, and 3 for 21 days. The blood from 9 subjects (group B) was collected in plastic bags (acid-citrate-dextrose blood pack), containing 75 ml. of acid-citrate-dextrose solution, U.S.P. formula A. These likewise were stored for periods of 7, 14, and 21 days. Blood was drawn from 9 subjects, group C), passed through a cation-exchange resin, and then stored in a plastic container (ion-exchange blood pack) for periods of 2, 5, and 10 days. The shorter time intervals were selected for this group because 10 days is the upper limit of cell survival under these conditions.

At the completion of the various periods of storage the blood was removed from the refrigerator. A sample of the blood was taken for analysis, and the remainder of the blood was passed through a resin column. The resin columns used consisted of 50 Gm. of Dowex 50-X8, sodium cycle, supported on 100-mesh nylon bolting cloth, in a vinylite casing. The columns were connected to the blood containers. The cold blood was passed over the resin at room temperature to simulate conditions prevailing during most clinical transfusions.

It was found that there is a progressive increase in ammonium and plasma potassium in blood stored in siliconized vacuum bottles and plastic containers. These ions accumulated more rapidly in blood decalcified by passage through an ion-exchange column than in blood to which acid-citrate-dextrose solution has been added. Passage of stored blood across a cation-exchange resin consistently reduced the concentrations of plasma potassium and blood ammonium to, or below, normal levels. This reduction was accompanied by a small increase in the plasma sodium concentration. This simple method is recommended as a means of effectively removing excessive potassium and ammonium from bank blood prior to transfusion.

Dispensability of Post-Operative Penicillin in Septic-Hand Surgery. J. Anderson. Brit. M. J. 2:1569-1571 (Dec. 27) 1958 [London].

In an attempt to evaluate the common use of penicillin after surgical interventions on septic lesions of the hand, the author studied the postoperative care given to 357 outpatients with sepsis of the hand. Of the 357 patients, 106 did not receive any chemotherapy, 110 were given penicillin orally, 104 received penicillin by intramuscular route, and 37 were excluded from the study because of complications, failure to return for dressings, or chronic infections. The types of the lesions in the 320 patients included paronychia in 102, onychia in 31, pulp abscess in 82, other abscesses in 94, and septic blister in 11. The respective healing times in the 3 unselected postoperative treatment groups were 9.4, 9.5, and 9.2 days.

The reduction in the over-all average healing time of less than a quarter of a day in the patients receiving penicillin by intramuscular route as compared with the group receiving no chemotherapy, under the conditions of the study, does not justify the administration of penicillin postoperatively without a special reason. Careful clinical examination, accurate diagnosis, and precise surgical intervention are of greater importance than routine chemotherapy. Routine postoperative administration of penicillin does not hasten healing in septic lesions of the hand which require surgical treatment, provided that a careful technique is based on anatomically accurate diagnosis. Penicillin has been safely excluded from the postoperative environment of uncomplicated acute infections of the hand, and this may be a more fundamental counter to the emergence of resistant organisms than recourse to other antibiotics. Possibly web abscess and threatened infection of the structures that move or support the hand are the only firm indications for chemotherapy, which will not act as a cover for erroneous diagnosis or inappropriate surgical intervention.

A Six Year Study of Incompatible Blood Transfusions. L. S. Binder, V. Ginsbert and M. H. Harmel. Surg. Gynec. & Obst. 108:19-34 (Jan.) 1959 [Chicago].

At the Kings County Hospital Center, Brooklyn, N. Y., 81,392 blood transfusions were administered during the 6-year period from 1952 to 1957. This study is concerned with observations on the 30 patients who received transfusions of improper blood. In 28 of these 30 patients it was proved that incompatible blood had been transfused. Twenty-six of the incompatibilities were in the ABO antigen system and 2 in the Rh system. The nature of the incompatibility could not be established in the remaining 2 patients, but as they had clinical and laboratory evidence of hemolysis, they are included in this series. The total incidence of incompatible blood transfusions in this hospital center was 1:2,713 (30:81,392). This figure differs from the incidence of hemolytic transfusion reactions, because 12 of the 30 patients did not have such a reaction. Of the 18 patients who were proved to have had a hemolytic transfusion reaction (an incidence of 1:4,520), 7 patients died, but in 5 of them the appearance of a coagulation defect contributed significantly to the deaths.

Although the role of renal ischemia in the pathogenesis of renal failure cannot be ruled in or out, the clinical parameters generally associated with decreased renal blood flow, i. e., shock and blood loss, could not be correlated with the production of kidney shutdown. Four phases have been differentiated in the clinical course of hemolytic transfusion reaction: an initial phase of clinical symptoms;

the interval phase of apparent clinical improvement associated with oliguria; the phase of renal failure identified with stupor, convulsions, and coma; and the phase of recovery heralded by the abrupt onset of diuresis. Each is variable in severity and duration, and one or more may be either clinically insignificant or lacking entirely. As the patient progresses through each phase, the therapy is varied to meet the changing clinical problem.

It was impressive how efficacious the high-calorie, protein-sparing, fluid-and-potassium-limited diet was in preventing uremia. Pulmonary edema and congestive heart failure due to hypernatremia and overhydration did not occur. Hyperkalemia may have been of clinical importance in one patient, and only in this instance might hemodialysis or peritoneal dialysis have been a necessary procedure. Once diuresis occurred, fluid administration was increased to match the output. To prevent dehydration and hypochloremia, attention was directed to sodium and chloride replacement.

In spite of vigorous treatment of patients in whom hemorrhagic diathesis developed, the results were eminently unsatisfactory. Therapy was directed toward 3 goals: (1) restoration or maintenance of the blood volume by energetic transfusion; (2) support of the blood pressure when necessary with vasopressors; and (3) correction of the clotting defects with fibrinogen, fresh-frozen plasma, or whole blood newly withdrawn. Yet none of the patients treated in this manner survived. The causes of incompatible blood transfusions and measures for reducing them are evaluated.

GYNECOLOGY & OBSTETRICS

Intrauterine Bacterial Infection of the Newborn Infant: Frozen Sections of the Cord as an Aid to Early Detection. K. Benirschke and S. H. Clifford. J. Pediat. 54:11-18 (Jan.) 1959 [St. Louis].

The authors report the histories of 2 newborn infants, illustrating bacterial infection of the fetus as an important cause of perinatal mortality and morbidity. While prolonged rupture of the membranes and prolonged labor are frequently associated with fetal infection, it may occur with intact membranes and be absent in instances of prolonged rupture. Fetal infection is probably acquired through an ascending infection of the amniotic cavity. According to the authors' experience, the fatal cases of fetal infection have all been associated with inflammation of the amniotic sac.

The frozen-section method described has proved to be a rapid and reliable means of determining, in suspected cases, the presence or absence of cord vasculitis. It frequently demonstrates the presence of actual organisms. The absence of inflammation may under certain circumstances suggest a viral infection. Frozen sections of the cord may enable the clinician to exert better judgment as to what method of treatment should be used. The indication for active treatment may be lifesaving for many infants days before the appearance of obvious clinical signs.

X-Ray Pelvimetry. E. A. Graber, H. R. K. Barber and J. J. O'Rourke. Am. J. Obst. & Gynec. 77:28-33 (Jan.) 1959 [St. Louis].

More than 200 different methods of x-ray pelvimetry have been advanced in the past 58 years. According to its advocates, modern roentgenologic pelvimetry has almost achieved the ultimate in accuracy and usefulness. This study scrutinizes the validity of this belief. Since practically all pelvimetric x-ray examinations in New York are interpreted and reported by roentgenologists, it was decided that the best way to arrive at an unbiased conclusion was to get pelvimetry reports from many different roentgenologists. This report is based upon 242 pelvimetries and deliveries. Roughly, this represents about 15% of the total number of deliveries. The methods of roentgenologic evaluation utilized were those of Thoms, Ball, Snow, Colcher and Sussman, and Caldwell and Moloy. These are the popular techniques in New York and are all about equal in accuracy. The indications for x-ray pelvimetry in this series were rather loose. The intention was to get as wide a sampling as possible of normal and abnormal pelves. Some of the x-rays were taken about one week from term, and some were taken when the patient was in labor.

The 242 roentgenologic pelvimetries, which were made by 18 different roentgenologists, were reviewed with regard to the prognostic accuracy of the reporting physician. Three out of 4 were reported correctly, but almost all of these were in the adequate pelvis with an average-sized baby. Since the roentgenologist has no method of measuring the fetal head adequately, he was in error most frequently in cases in which the obstetrician needed help—cases of cephalopelvic disproportion due either to a borderline pelvis or to an unsuspected larger baby in an average pelvis.

It is suggested that the roentgenologist does not usually have sufficient information or the obstetric background to make a clinical prognosis and should cease predicting the outcome of delivery. Furthermore, by his predictions, he places the obstetrician in an untenable position medicolegally. X-ray pelvimetry was never intended to take the place of an adequate pelvic examination in labor, and a trial of labor. It is a laboratory aid at best and should be used as such. Roentgenologic pelvimetry should be limited to 2 situations: (1) malpresentation, and (2) lack of adequate clinical progress in labor. The authors feel that x-rays should be taken only while the patient is in labor for maximum information. Since all radiation is harmful, all routines as to the number of plates should be discarded. A specific minimum number of views should be ordered by the obstetrician for the individual patient.

Megaloblastic Anaemia of Pregnancy and the Puerperium. C. Giles and E. M. Shuttleworth. Lancet 2:1341-1347 (Dec. 27) 1958 [London].

Of 3,199 pregnant women who were delivered at the City General Hospital in Stoke on Trent, England, and at the allied Limes Maternity Hospital, between March 1, 1957, and May 31, 1958, 474 with an arbitrary hemoglobin level of 9.5 Gm. per 100 cc. (65%) or less were studied by sternal puncture. Of the 474 patients, the bone marrow was found to be megaloblastic in 90 and normoblastic in 372; in the remaining 12 patients megaloblastic anemia was suspected, but a firm diagnosis could not be established. In 28 of the 90 patients with megaloblastic anemia, the megaloblastic marrow was found in the puerperium. Seventy-two (80%) of the 90 patients, whose average age was 28.9 years, were multiparas, and 7 (7.8%) of the 90 gave birth to twins, as compared with 9 twin deliveries (2.4%) among the 372 patients with normoblastic anemias, thus confirming previous reports of the higher incidence of megaloblastic anemia in multiple pregnancies. In patients with a hemoglobin level of less than 6.5 Gm. per 100 cc. (45%), the anemia was more frequently megaloblastic than normoblastic.

Of 67 patients in whom test meals were carried out, 26 (37%) had achlorhydria, and fat absorption was impaired in 4 patients. No special seasonal incidence of megaloblastic anemia was noted. Gastrointestinal symptoms were uncommon, and the incidence of complications, such as preeclamptic toxemia and obstetric hemorrhage, was not substantially higher among the patients with megaloblastic anemia than among those with normoblastic anemia. In 38 (42%) of the 90 patients with megaloblastic anemia, the diet was poor, compared with 12% on a similar diet among the patients with normoblastic anemia and 4% among healthy controls. The difference was even greater, when the intake of meat was compared. No local factors could be discovered to account for the high incidence of megaloblastic anemia in this series. All the patients were treated with folic acid. The reticulocyte peak and the drop in the serum iron level reflected the response to treatment in most of the patients.

Survival of Female Patients with Cancer of the Breast: A Study of the Effects of Demographic and Economic Factors. B. D. Waxman and W. T. Fitts Jr. Am. J. Surg. 97:31-35 (Jan.) 1959 [New York].

Of 633 women with a pathological diagnosis of cancer of the breast, who were treated primarily at the Hospital of the University of Pennsylvania in Philadelphia between 1943 and 1951 and whose average age was 53.7 years, 67% were married, 16% were widowed, 13% were single, and 4% were divorced. Thirty-six per cent were ward patients, 46% occupied semiprivate rooms, and 18% were in private rooms. The type of room patients occupy in a hospital is probably a good index of their economic condition. Analysis of the relationship between economic status, as measured by the type of room occupied, and the duration of symptoms at the time the patient reported them revealed striking differences. While only 20.6% of the ward patients reported their symptoms within one month, 36.2% of the private patients reported their symptoms early. This difference is significant and is considered strong evidence that economic status is positively correlated with early reporting of symptoms. A significant increase was noted in the proportion of ward patients reporting symptoms of one month's duration in the period from 1947 to 1951 as opposed to the period from 1943 to 1946. This finding indicates that publicity about cancer is having a significant effect in reducing the duration of symptoms for the lower economic strata.

Of 191 women with cancer of the breast who were followed up for 5 years, 67% of those with a duration of symptoms of less than one month survived 5 years, as opposed to 60% with a duration of symptoms of 1 to 2 months, 56% with a duration of 3 to 5 months, 45% with a duration of 6 to 9 months, and 37% with a duration of 10 months and more. These data indicate that patients who report cancer symptoms early have a better chance of survival. Although the authors did not demonstrate a statistically significant relationship between economic status and survival when the Chi-square test was employed, the reported observations suggest that there may be an economic factor working indirectly on survival through a differential time lag in the reporting of symptoms.

PEDIATRICS

An Appraisal of Fulminant Meningococcemia with Reference to the Shwartzman Phenomenon. W. Margaretten and A. J. McAdams. Am. J. Med. 25:868-876 (Dec.) 1958 [New York].

Of 52 children with fatal meningococcic infection who died at the Cincinnati Children's Hospital between 1937 and 1956, autopsies were performed on 40. The meningococcus organism was identified by culture or smear in 34 of these 40 patients, and in the remaining 6 autopsy revealed the classic features of the Waterhouse-Friderichsen syndrome, as well as the typical purpura of meningococcemia. The adrenal glands were examined in the course of autopsy in all 40 patients and were considered to be typical of the Waterhouse-Friderichsen syndrome in all but 4 patients in whom purulent meningitis was the cause of death. Sections of kidney also were studied in all 40 patients. Thrombi, either glomerular, intertubular capillary, or both, were observed in 9 patients. In 3 of these patients there was also bilateral cortical necrosis. These 3 patients were not in shock at the time of admission to the hospital and received some form of adrenocortical steroid before the development of shock, suggesting a direct relationship of the renal cortical necrosis to adrenal steroid therapy. This occurrence and the apparent causal relationship of thrombosis in the production of the hemorrhagic lesions of the skin and adrenals in the Waterhouse-Friderichsen syndrome suggest that the Shwartzman phenomenon may be responsible for certain manifestations of fulminant menigococcemia. The apparent rarity of renal cortical necrosis in meningococcic infection in man, a lesion that is characteristic of the generalized Shwartzman reaction in rabbits, suggests that the common skin and more occasional adrenal lesions of this disease may be produced by the local Shwartzman phenomenon.

The cases of the 52 children with fatal meningococcic infection were compared with 152 consecutive bacteriologically proved cases of meningococcemia in which the patients survived. Of the 204 patients, virtually all received intensive antibacterial therapy, but only 63 received some form of adrenal steroid therapy. Considering only the 166 patients who were not presumed to be in shock at the time of admission, there was a striking difference in outcome: the mortality rate among the patients receiving steroid therapy was 21% as compared with a 7% mortality rate among those not so treated. These observations, as well as those in the 3 patients with fatal meningococcemia and bilateral renal cortical necrosis, imply that a deleterious rather than a beneficial effect may result on occasion from the use of adrenal steroid therapy in patients with fulminant septicemia.

Enteroviruses and Diarrhoea in Young Persons. R. G. Sommerville. Lancet 2:1347-1349 (Dec. 27) 1958 [London].

During one year from April, 1957, a single stool specimen was obtained on admission from each of 338 children, all aged 5 years or less, who were admitted with diarrhea to the Ruchill Hospital in Glasgow. Seventy-five enteroviruses were isolated from the stool specimens of these patients, and 17 enteroviruses were isolated from the stools collected from 115 children of similar age, admitted with respiratory infections to the same hospital during the same period and serving as controls. The proportion of poliomyelitis viruses and Coxsackie viruses was similar in the children with diarrhea and in the controls, but the number of enteric cytopathogenic human orphan (ECHO) viruses isolated from the children with diarrhea was greater (although not significantly) than in the controls. The enteroviruses isolated included 3 types of poliomyelitis virus, Coxsackie B1, B3, and A9, and ECHO 6, 7, 9, 11, and 13. The most frequently observed types were ECHO 7, Coxsackie A9, and poliomyelitis 1. In 23 patients an enterovirus and a pathogenic bacterium were isolated from the same stool specimen. The commonest combination consisted of Shigella sonnei and either ECHO 7 or Coxsackie A9. A virus was isolated from 22%, and a specific intestinal pathogenic bacterium from 36.5% of the children with diarrhea, making a total isolation rate of 58.5% for the whole group of 338 children. The total isolation-rate, considered in relation to the ages of the patients, was lowest (44.5%) among children aged less than 1 year, but averaged 80% among children between the ages of 1 and 5 years.

Heart Failure in Infants. K. Simpson. Proc. Roy. Soc. Med. 51:1022-1023 (Dec.) 1958 [London].

The records of 50 infants admitted to the hospital with heart failure were reviewed to determine early signs of failure and to assess the incidence of respiratory infection. The reason for referral was noted in 40 infants. Although 26 of these were in failure when they were first seen, a diagnosis of heart failure was made in only 1 before admission. In two-thirds of the infants heart disease had not previously been suspected, diagnoses implying respiratory disease or feeding difficulty being made. Regarding the final diagnoses, the author states that in 10 infants no congenital cardiovascular anomaly was detected, whereas in the other 40 infants heart failure occurred with congenital heart disease. In 6 of the 10 infants without congenital defect, heart failure developed with acute pulmonary infection; in 4 infants failure was associated with cardiac arrhythmia. Nineteen of the 40 infants with congenital heart disease had lesions for which operation offers, or may soon offer, a prospect of improvement or cure (venticular septal defect, patent ductus arteriosus, pulmonary stenosis, coarctation of aorta, and tetralogy of Fallot); 14 of these 19 infants have recovered from heart failure.

Enlargement of the liver was a frequent clinical feature, being present in 40 of the infants. Respiratory disturbances were noted in 42. Tachypnea at rest was an early sign of cardiac failure and often preceded hepatomegaly by many hours, the respiratory rate rising rapidly and progressively. Cardiac enlargement was found in 27 infants. Venous distention was seen in 14 infants. Indisputable edema was present in 12 infants. In 5 of these, heart failure was not associated with congenital heart disease, and all recovered. The remainder, who had congenital cardiac anomalies, died. Rales were heard in 27 infants. When tachypnea is associated with fever or with pulmonary rales in an infant who has congenital heart disease, the differentiation of heart failure from respiratory infection is extremely difficult, and the 2 conditions frequently coexist.

The assessment of infection was based on the history, occurrence of coryza, presence of pulmonary rhonchi, clinical pathological data, and roentgenologic and postmortem evidence. No evidence of infection was found in 21 cases; 14 infants in this group died, the majority having severe and complicated malformations. Of 20 infants with respiratory infection, 9 died; 6 of these had cyanotic congenital heart disease. In the remainder pulmonary consolidation or collapse was found. The overall mortality was 48%. Fifteen out of 16 infants, with right-to-left shunts large enough to produce cyanosis, died, the presence of respiratory infection making little difference to the outcome. Of 24 infants with acyanotic congenital heart disease, 8 died. In this group infection probably played a bigger part in precipitating failure.

Prematurity and "Cerebral Palsy." P. E. Polani. Brit. M. J. 2:1497-1499 (Dec. 20) 1958 [London].

That there is an association between prematurity and cerebral palsy impressed the earliest students. The nature of this association is not clear, but the author shows that for some investigators the effect of prematurity is to cause a developmental anomaly of the pyramidal tracts; for others, the two conditions are parallel manifestations of an intrauterine abnormality causing both prematurity and primary antenatal degeneration of cerebral neurons. Since cerebral palsy is an aggregate of clinical syndromes with various origins, the author suggests that one might expect some types of cerebral palsy to be more strongly associated with prematurity than others.

Reviewing the incidence of prematurity in various clinical types of cerebral palsy, the author found a particularly strong association with 2 neurological syndromes: (1) dystonic/choreoathetoid cerebral palsy after severe neonatal jaundice not due to blood-group incompatibility, and (2) cerebral spastic [illegible]. The possible mechanisms [illegible] are considered, and a selective developmental origin for the neurological troubles is favored tentatively. Because of the association between retrolental fibroplasia and cerebral spastic paraplegia/diplegia, and because of the clinical features of the cerebral spastic paraplegia syndrome without history of perinatal or postnatal troubles, a postnatal interference with development is the mechanism postulated for this clinical type of cerebral palsy. Although the suggestion that premature birth may at times cause postnatal interference in development and maturation of critically maturing neurons is entirely hypothetical, it can be put to the test by experiments with high-oxygen pressures in immature animals.

Spiramycin in the Clinical Treatment of Infants. P. Caruso and S. La Rocca. Clin. pediat. 40:663-687 (Aug.) 1958 (In Italian) [Bologna, Italy].

A study on the effect, in vitro and in vivo, of spiramycin is reported. In vitro, the drug proved very effective in inhibiting hemolytic and fecal pneumococci. The clinical study was made on 24 children, between the ages of 5 months and 11 years, with acute bronchopneumonia. Spiramycin was administered in an initial dosage of 100 mg. per kilogram of body weight per day, divided into 2 or 3 equal subdoses and combined with large quantities of vitamin C and vitamin B complex. Eight of the children had been treated previously with other antibiotics but with no beneficial effect. The spiramycin therapy was followed by clinical recovery in all the children. There was a drop in temperature 24 to 72 hours after the beginning of treatment; in only one child did a high temperature persist for 6 days. Clinical symptoms regressed after 2 to 8 days of treatment. Recovery was faster in those children who had been treated previously with other antibiotics. Spiramycin had no toxic effect and was well tolerated by all the patients.

Large Abdominal Lumps in Children with Particular Reference to Embryoma of the Kidney: A Survey of 100 Consecutive Cases. J. H. Louw. Med. Proceed. 4:801-809 (Dec. 13) and 832-837 (Dec. 27) 1958 [Johannesburg, South Africa].

Discussing the general problem of large abdominal tumors in childhood, the author gives particular attention to Wilms's tumor, pointing out that embryoma of the kidney (nephroblastoma) has been most aptly described as "a tremendous tumor with a tiny child attached to it." The author reviews observations on 100 consecutive children who presented with large abdominal masses at the children's surgical units of Groote Schuur Hospital and the Red Cross Children's Hospital of the University of Cape Town over the past 7 years. Nearly half of the 100 children with large abdominal lumps had malignant disease, and nephroblastoma accounted for half of these. Malignant disease is not uncommon in childhood, and its possible existence should constantly be borne in mind. The age group of 1 to 4 years appears to be particularly prone to malignant disease. In considering the 100 children with abdominal swellings, the incidence of malignant swellings in this group was 8 times greater than that in infants under 1 year, and 4 times that in children of 5 years and over. In the age group of 6 months to 6 years, almost 80% of the swellings were malignant. More than 95% of the abdominal malignancies occurred in this group, and so did all the nephroblastomas in this series. In the group ranging in age from birth to 6 months, most of the swellings were due to serious congenital malformations. In the group 6 years of age and over, chronic inflammation and benign tumors and cysts accounted for 75% of the swellings.

Early diagnosis depends first on routine palpation of the abdomen of every child who is brought for any examination. If an abdominal lump is found, intravenous pyelography is usually necessary. Exploratory laparotomy should be performed on all children in whom a neoplasm is suspected or when there is doubt about the diagnosis. The prognosis of malignancy in children is unfavorable; if it occurs in the abdomen, less than one-third of the children survive 5 years. This applies particularly to nephroblastoma. Surgical removal still offers the best chance of survival, particularly in nephroblastoma. Radiotherapy is a valuable adjunct to surgery and should always be used in nephroblastoma. Chemotherapy is of limited value.

UROLOGY

Endocrine-Control Therapy in Prostatic Cancer. J. D. Fergusson. Brit. J. Urol. 30:397-406 (Dec.) 1958 [Edinburgh].

The author reviews observations on 344 consecutive patients with prostatic cancer treated by him over a period of years extending to January, 1958. Urinary symptoms directly referable to the primary growth were observed in 262 of the 344 patients; 55 patients had metastatic manifestations, and a further 9 had a combination of the two. Of the remaining 18 prostatic cancers, some were brought to light on routine rectal examination and a small number by the discovery of cancer in material removed by enucleation prostatectomy. Clinically, 264 patients gave positive evidence of disease at the primary site, while in 80 the rectal findings were negative or equivocal. The diagnosis was confirmed histologically or cytologically in 288 patients and, in the remainder, by the presence of strong clinical evidence supported by roentgenologic and serologic findings. The 288 patients were treated initially with estrogens, supplemented by conservative transurethral resection (when indicated) for the relief of urinary obstruction. Fifty-six patients received no hormones but were otherwise similarly treated. Most of the latter were early cases, and, with the possible exception of 8 patients who could not be traced, all were known to have died before January, 1958. Of the 288 who received hormone therapy, 207 have died, while 81 are surviving.

As a result of his experience with various methods of endocrine-control therapy, the author arrives at the following conclusions: 1. Endocrine-control therapy is selective in action and is insufficient to eliminate prostatic cancer. 2. Approximately 20% of cancers are resistant to the simpler forms of treatment (estrogen therapy and castration). 3. Failure to respond to one form of therapy does not necessarily preclude a response to others, but appears to make this less likely. 4. Different parts of the same tumor may react differently, and this applies also to the primary growth and its metastases. 5. There is no reliable index of hormone sensitivity, and the only prognostic data of value are age and the presence or absence of disseminated disease.

Influenced both by the survival studies and clinical considerations, the author is inclined to advocate initial treatment with high doses of estrogens in all active cases, supplemented where necessary by castration. No treatment is indicated for latent cancer. Subsequent adrenalectomy for relapse or resistance has been abandoned, as the results generally fail to offset the inconvenience of treatment. "Irradiation hypophysectomy," representing an attack on the fountainhead and offering less of an ordeal, is now preferred, but it still remains too uncertain to be used as a primary definitive treatment. Judicious application of endocrine therapy can do more to mitigate suffering in disseminated prostatic cancer than any other method presently at disposal.

Chemotherapy of Renal Tuberculosis. H. Wechsler, J. K. Lattimer, M. A. Garcia and H. Kavookjian. New York J. Med. 59:49-52 (Jan. 1) 1959 [New York].

The authors report on the effectiveness of 3 regimens, with isoniazid, streptomycin, and aminosalicylic acid, in treating patients with renal tuberculosis at the research unit for genito-urinary tuberculosis of the Bronx Veterans Administration Hospital in New York. The results of triple-drug therapy, with isoniazid in doses of 100 mg. 3 times daily, sodium aminosalicylate in doses of 5 Gm. 3 times daily, and streptomycin in doses of 1 Gm. twice weekly, for one year were encouraging (a report on this treatment was published in THE JOURNAL, Feb. 18, 1956, page 544). Less effective were single drug regimens with streptomycin or isoniazid alone. A two-drug regimen with 1 Gm. of streptomycin twice a week and 12 Gm. of sodium aminosalicylate daily was also less effective. Follow-up studies have shown the value of triple-drug treatment. After streptomycin was given alone, patients suffered relapse at a prohibitive rate, with only about 20% of the patients showing conversion of urine cultures to negative by the 5th year of follow-up. The follow-up of patients given streptomycin–aminosalicylic acid therapy revealed a drop to 70% in successful conversions by the 6th year, while 24 (96%) of 25 patients on the three-drug regimen have maintained conversions for 4 years.

Continued observation of the patients for at least 10 years may indicate the optimum therapeutic regimen among the several combinations now under study. Two-drug therapy may be used for lesions of small volume (groups 0 and 1 according to the classification of Lattimer). The advanced cavitary lesions (groups 2, 3, and 4) are now treated with triple-drug therapy—100 mg. of isoniazid 3 times daily, 5 Gm. of sodium aminosalicylate 3 times daily, and 250 mg. of cycloserine twice daily. This treatment is given for 2 years. The patient is usually kept in the hospital during the first 6 to 12 months, but treatment is continued for a second year after his discharge. A semiambulatory rest program is encouraged during the first 6 months of treatment, and rest is encouraged each day. The year in the hospital is also used for rehabilitation and job training for the future. The use of monoxychlorosene, a hypochlorous acid derivative (Clorpactin 90), for local bladder therapy is a helpful adjuvant in relieving the pain from tuberculous ulcers of the bladder. Two new drugs, kanamycin and thiocarbanidin, are now under trial to serve as substitutes for drugs which are difficult to tolerate (aminosalicylic acid) or require injection (streptomycin). The authors have withheld surgical treatment even for patients with advanced renal tuberculosis and will continue to do so unless relapses occur.

THERAPEUTICS

Clinical Research on the Analgesic Action of 2,2-diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine in Dextrose Solution (R 875). A. Pesce, M. Ricciardi and G. Rugiero. Policlinico (sez. prat.) 65:1766-1770 (Nov. 17) 1958 (In Italian) [Rome].

Sixty-two obstetric-gynecologic patients benefited from the analgesic action of 2,2-diphenyl-3-methyl-4-morpholinobutyrylpyrrolidine in dextrose solution (R 875). R 875 was given in several doses of 1 or 2 mg. every 5 to 10 minutes, as a complementary analgesic drug to thiobarbituric acid, to 25 obstetric-gynecologic patients during a surgical operation. This procedure permitted the maintenance of anesthesia during operations lasting more than 2 hours without any further administration of thiobarbituric acid. Twenty-five gynecologic patients received subcutaneously or intramuscularly 5 to 10 mg. of R 875 during 71 episodes of acute postoperative pain after return to consciousness. [These patients had not received R 875 during the operation.] The analgesic effect of R 875 was more intense, and it developed earlier and lasted longer (between 4 and 6 hours altogether) than that of morphine, meperidine hydrochloride, or methadone hydrochloride which were used on other occasions. R 875 was given intramuscularly to 12 women during labor in doses of 10 mg. every 20 to 30 minutes until the threshold of anesthesia was reached. The drug induced an intense analgesic state without affecting mental lucidity of the patients. This effect permitted a cooperative attitude of the parturients during expulsion and reduced the duration of labor. Oral or subcutaneous administration of R 875 produced mild side-effects: pallor, malaise, and nausea accompanied by vomiting. Intravenous administration of the drug brought about more serious side-effects: rapid vertical and horizontal clonic motions of the eyeballs and respiratory disturbances, including apnea. Therefore, it is suggested that the intravenous administration of R 875 be carried out only under the supervision of an anesthetist.

Digestive Hemorrhages and Gastroduodenal Ulcers Caused by Aspirin (with Special Reference to Fifty-two Personal Observations). M. Levrat and R. Lambert. Presse méd. 66:1945-1948 (Dec. 10) 1958 (In French) [Paris].

Mild reactions from digestive intolerance to aspirin are considered banal, but severe digestive complications are not regarded as commonplace. The authors believe that aspirin provokes isolated digestive hemorrhages and is the drug most frequently responsible for ulcerous hemorrhages. Their work is based on observations of 52 patients made in 1957 and 1958. Digestive disturbance usually took place a few hours after the absorption of aspirin, usually within 24 hours. Thirteen of the patients had an ulcerous nonhemorrhagic attack, and in 2 of them the disturbance lasted for several months. In 39 of the patients aspirin caused digestive hemorrhage of the following 3 types: in 15 cases there was roentgenologic proof of an active ulcer; in 21 cases the hemorrhage was isolated and not related to any evident digestive lesion; and in 3 cases there were signs of alcoholic hepatitis.

Ulcerous "terrain" plays a large part in the genesis of these disorders. Altogether 78% of the 52 patients in this series had an ulcerous condition. In 16 of the patients the histaminopexic (histamine-fixing) power was absent in the serum and in the gastric juice. Aspirin occasionally promoted chronic dyspeptic trouble. It provoked reactivation of ulcer without hemorrhage in 13 patients, maintained an ulcerous condition in 2, and caused a perforation in 1. *Digestive hemorrhage is the most frequent* type of digestive disorder from aspirin and was present in 75% of the authors' series. It usually has a benign course. Some statistics are cited, indicating that aspirin is responsible for one-third of ulcerous hemorrhages and for about one-half of isolated digestive hemorrhages, but the series was too small to be entirely reliable.

The pathogenic mechanism of the disturbance caused by aspirin proceeds from the corrosive action of the gastric contents combined with the presence of insoluble particles. The action is general and is harmful to a predisposed mucous membrane. Experiments by the authors on 200 rats resulted in superficial and hemorrhagic lesions of the gastric mucosa after oral or parenteral administration of aspirin. There is a possibility of neurohumoral reaction being a responsible factor. The effect of aspirin on the blood crasis and on the hemostasis process favors the hemorrhagic character of the disturbance. Persons with ulcerous "terrain" should be dissuaded from using aspirin.

The Hypocholesterolemic and Plasma-Clearing Action of a New Heparinoid Extractive Free from Anticoagulant Effects. L. Sereno and A. D. Peruzy. Minerva med. 49:4195-4201 (Nov. 14) 1958 (In Italian) [Turin, Italy].

A new Italian heparinoid extractive free from anticoagulative effects, Ateroid, was given to 42 patients of both sexes with high serum cholesterol and lipoprotein levels. One group consisting of 20 patients who had patent organic lesions of the cardiovascular system had one or another of the following diseases: myocardial sclerosis, chronic coronary disease, or aortic or arteriosclerotic generalized lesions alone or associated with arterial hypertension. The other group of 16 patients did not have patent cardiovascular lesions but had a marked disorder of the lipid metabolism and were affected by one of the following conditions: xanthomatous obesity, xanthelasma, cholelithiasis, nephrosis, or essential hypertension. The drug was administered orally after meals to 37 patients in daily doses of 60 mg. divided into 6 equal tablets for a period of 30 to 50 days. Five patients received the drug intramuscularly in doses of 20 to 40 mg. a day for the same period of time.

Serum cholesterol levels decreased in patients with patent cardiovascular lesions from basal values of about 272 mg. per 100 cc. to about 240 mg. per 100 cc. after 20 days, and they reached about 255 mg. per 100 cc. after 30 days of drug therapy. Serum beta to alpha lipoprotein ratios decreased from basal values of about 4.95 to about 3.43 after 30 days of drug therapy. These values remained low in some patients and returned to the basal ones in the remainder after a prolonged period of observation. Similar results, although to a slighter extent, were observed in patients without patent cardiovascular lesions. Serum cholesterol levels decreased from basal values of about 307 mg. per 100 cc. to about 282 mg. per 100 cc. after 20 days and to about 243 mg. per 100 cc. after 30 days of chemotherapy. Serum beta to alpha lipoprotein ratios decreased from basal values of about 5.45 to about 4.44 after 30 days of drug therapy.

Ateroid thus exerted a similar hypocholesterolemic and plasma-clearing effect in both groups of patients, except that it lowered the beta to alpha lipoprotein values in the first group of patients by 31% and in the second group by only 18%. Both oral and intramuscular administration of Ateroid produced similar results. The drug was well tolerated and produced no side-effects.

Use of a Tranquilizing Agent (Hydroxyzine) with Prednisolone in the Control of Allergic Disorders. J. L. Fox. Ann. Allergy 16:674-677 (Nov.-Dec.) 1958 [St. Paul].

Corticosteroids administered in combination with tranquilizing agents have been reported superior to corticosteroid therapy alone in the management of nonallergic disorders influenced by anxiety. The study reported here was designed to test whether this type of adjunctive tranquilizer therapy is likewise superior to steroid therapy alone in the treatment of various allergic disorders. The study was restricted to patients with bronchial asthma, allergic rhinitis, urticaria, or seasonal hay fever, and included only those whose previous course suggested that short-term corticosteroid therapy was indicated. These criteria were fulfilled in a total of 67 patients, 11 of whom were children under 12 years of age. As individual patients were seen, they were arbitrarily assigned to one of 2 treatment groups: patients in one group received prednisolone together with a tranquilizing agent (hydroxyzine), while patients in the other group received only prednisolone. In order to achieve a high degree of objectivity in evaluating the response of these patients, the study was conducted under double-blind conditions.

Significantly better control of symptoms was achieved by the prednisolone-hydroxyzine combination than by prednisolone given alone. No significant side-reactions were observed in patients treated with the combination; on the other hand, it was necessary to discontinue therapy in 12% of the prednisolone-treated patients because of reactions to the drug. The combination of hydroxyzine with prednisolone appears from these results to offer advantages over corticosteroid therapy alone in the short-term symptomatic treatment of bronchial asthma and other allergic disorders.

On a New Synthetic Cortisonic Substance, Dexamethasone (16-alpha-methyl-9-alpha-fluoroprednisolone), in the Treatment of Rheumatoid Arthritis. A. Robecchi, V. Daneo, S. Di Vittorio and others. Minerva med. 49:4163-4171 (Nov. 10) 1958 (In Italian) [Turin, Italy].

The effect of dexamethasone (Decadron) was studied in 22 patients, 7 male and 15 female, between 26 and 69 years of age, with rheumatoid arthritis. Two patients had received no previous treatment with steroids, 16 had been treated previously with steroids but the treatment had been discontinued for at least one month, and 4 patients were being treated with other steroids when treatment with Decadron was begun. The diet of the patients was not changed. The initial dose of Decadron ranged from a minimum of 1.6 mg. per day in 5 patients to 3 mg. per day in 3 patients. Each daily dose was divided into 3 or 4 subdoses given every 8 or 6 hours per day respectively. Maintenance dose ranged from a minimum of 0.75 mg. per day to a maximum of 2 mg. per day. Decadron had a beneficial effect on all the general and local symptoms: the relief of symptoms was similar to that obtained in treatment with prednisone. Suspension of the treatment caused a regression in the improvement obtained. Subjective symptoms were checked mostly within the first few days of treatment, and some beneficial effect could be noticed within 24 hours. A sensation of well being, increased appetite, gain in strength, disappearance of fever when present, and decreased erythrocyte sedimentation rate followed the relief of subjective symptoms. The behavior of the erythrocyte sedimentation, however, was not always parallel to the symptomatic improvement, and for this reason the authors believe that the optimal dose should be established by taking into consideration mainly the clinical condition of the patient; with patients in very serious condition it is difficult to obtain and maintain normal erythrocyte sedimentation values. From the clinical point of view Decadron had a very good effect on 10 patients; though symptomatic relief and clinical recovery were not complete, it was possible to reclassify these patients as having less severe forms of the disease. The results obtained in the remaining 12 patients were good; it was not possible to transfer these patients to a different functional class, but a marked improvement in their general condition and functional capacity was obtained. Decadron had no significant side-effects. A comparative study on the effect of Decadron and of other steroids showed that the relationship between the effect of Decadron and that of prednisone stood in the proportion 1 to 9; this effect was 1 to 8 in the case of triamcinolone. In one patient the clinical effect obtained with 1.5 mg. of Decadron was far superior to the effect obtained with a combination of 4.5 mg. and 150 mg., respectively, of prednisone and phenylbutazone.

PATHOLOGY

Carcinoid of the Appendix with Total Invagination of the Organ. G. Capitolo. Minerva chir. 13:1269-1274 (Nov. 15) 1958 (In Italian) [Turin, Italy].

A male patient, 34 years of age, was operated on for subacute appendicitis. At operation, the cecum appeared hyperemic. The appendix was completely turned inside out, like a finger of a glove, in the lumen of the cecum; the tunica mucosa formed the external side of the appendix, whereas the tunica serosa formed the internal side of the organ. The mesenteriolum was also hyperemic and intruded with the invagination of the appendix. An unsuccessful attempt to reduce the appendix to the normal condition was followed by resection of the mesenteriolum. The appendix was resected through a circular incision in the wall of the cecum at the site of the invagination. At microscopic examination, the mucous surface was ulcerated and contained granulation tissue full of lymphocytes, plasma cells, and necrotic cells of other types. Cords and nodes of epithelium cells, each with a globular, hyperchromatic nucleus and with frequent karyokinesis, were found in the mucosa, submucosa, and tunica muscularis. A diffuse, reactive lymphohistocytic hyperplasia in the stroma was observed. The histological diagnosis was invagination of the appendix affected by epithelioid neoplastic cells, which had varying features between carcinoid and anaplastic carcinoma. The patient was discharged on the 8th postoperative day and has been well for 3 years since operation.

Coronary Heart Disease and Physical Activity of Work: Evidence of a National Necropsy Survey. J. N. Morris and M. D. Crawford. Brit. M. J. 2:1485-1496 (Dec. 20) 1958 [London].

This report is one of a series. It continues the study of coronary (ischemic) heart disease in relation to physical activity of work. The hypothesis was previously stated that men in physically active jobs have a lower incidence of coronary heart disease in middle age than men in physically inactive jobs. More important, the disease is not so severe in physically active workers. All departments of morbid anatomy in the hospitals of the National Health Service of Scotland, England, and Wales were invited to take part in a national autopsy survey during 1954-1956 by sending particulars of the naked-eye findings on the coronary arteries, the myocardium, and other specified items for a consecutive series of 25 males, aged 45 to 70 years, coming to autopsy. About 5,000 reports were received, made up in round numbers thus: 1,200 deaths from coronary heart disease, etc. (group A); 1,000 deaths from conditions with a specially high prevalence of coronary artery disease—for example, deaths caused by hypertension and its complications, deaths in diabetics, deaths from arterial disease in other sites (group B); and, the remainder, 2,800 deaths from miscellaneous conditions, their main causes having no particular association with coronary artery disease (group C).

Two types of ischemic myocardial fibrosis in the left ventricle and interventricular septum are described: (1) the large, discrete, often solitary patch which is probably the end-result of major and acute infarction and is associated particularly with occlusion in a main coronary artery (90 cases among the 3,800 noncoronary deaths); and (2) smaller, commonly multiple scars, the result probably of more chronic and less severe ischemia, and occurring in hearts showing usually smaller focal narrowings of coronary arteries or branches (290 cases). Cases were classified as "hypertensive" or "other." About half of the patients in group B and 10% of those in group C were thus regarded as hypertensive. The large healed infarcts (type 1 fibrosis) were found equally in hypertensive and other patients; focal myocardial fibrosis of type 2 was commoner in hypertensive patients than in those without record or evidence of hypertension.

The last occupation of each man was graded on a three-point scale, in terms of the physical activity the job typically involved, as "light," "active," or "heavy." On the evidence obtained, the authors feel that the general hypothesis may be restated in causal terms that physical activity of work is a protection against coronary (ischemic) heart disease. Men in physically active jobs have less coronary heart disease during middle age, what disease they have is less severe, and they develop it later than men in physically inactive jobs. Since there are suggestions of other connections between physical activity of work and cardiovascular disease of middle age, and multiplying evidence from laboratory experiment of the beneficial effects of exercise on relevant cardiovascular physiology and pathology, the speculation may be advanced that habitual physical activity is a general factor of cardiovascular health in middle age. In the present material the hearts of sedentary and light workers showed the pathology of the hearts of heavy workers 10 to 15 years older. Coronary heart disease among heavy workers, though less common, less severe, and occurring later than among light workers, is nevertheless common enough to constitute a major health problem.

Mucocutaneous-Ocular Syndrome with Intestinal Involvement: A Clinical and Pathological Study of Four Fatal Cases. J. Bøe, J. B. Dalgaard and D. Scott. Am. J. Med. 25:857-867 (Dec.) 1958 [New York].

The designation "mucocutaneous-ocular syndrome" is used as a general collective term to include Behcet's syndrome, severe erythema exudativum multiforme, and the Stevens-Johnson syndrome. Usually the respiratory tract or the central nervous system is affected, and involvement of the gastrointestinal tract is not infrequent but has rarely been reported in the literature. This prompted the authors to report the history of 4 middle-aged women with the mucocutaneous-ocular syndrome and involvement of the gastrointestinal tract who were admitted to medical department B and the Gade Institute of the University Hospital in Bergen, Norway, between 1955 and 1957. The duration of the disease varied from 8 months to 15 years; the course was markedly remittent, although progressive. In 2 patients the main lesions were in the large intestine, associated with a clinical picture of ulcerative colitis. In one patient the lesions were confined for the most part to the rectum, and in the other the histological examination revealed that the entire gastrointestinal tract was involved, although gastrointestinal symptoms were not noted at all. The microscopic findings were chiefly limited to moderate, nonspecific, inflammatory reactions surrounding capillaries and venules. Sigmoidoscopy will not suffice to separate these cases from ordinary ulcerative colitis, but history of exanthem, recurring stomatitis, anogenital ulcers, and involvement of the eyes may be diagnostic. The observations in 2 patients indicated impaired wound healing, which suggests caution in surgical intervention.

The Latex-Fixation Test and the Lupus Erythematosus Cell Test: Investigations on Their Diagnostic and Etiological Significance in Primary Chronic Polyarthritis. H. Braunsteiner, F. Egghart, F. Reinhardt and G. Wiedermann. Deutsche med. Wchnschr. 83:2168-2170 (Dec. 5) 1958 (In German) [Stuttgart, Germany].

According to Braunsteiner and associates, the development of the latex-fixation test by Singer and Plotz in 1956 represented a definite advance in the diagnosis of rheumatoid arthritis (primary chronic polyarthritis). The test resembles the hemagglutination test, but instead of sensitized sheep erythrocytes, polystyrene-latex particles are employed. Latex solution is added to a series of test tubes containing progressive dilutions of patient serum. The authors slightly modified the technique suggested by Singer and Plotz in that, after centrifugation, the test tubes are allowed to stand for 24 to 48 hours, instead of reading the test results at once, as was done by Singer and Plotz. This has the effect that some tubes with higher dilutions have more time for precipitation, and some tests that at first showed negative reactions become positive. The authors also mention the modification suggested by McCoy and associates, the so-called droplet test, which saves gamma globulin as well as time. Although McCoy claimed that this modification had the exactness of the original test, Braunsteiner and associates found that the results were less exact. They tabulate the results they obtained with their technique of the latex-fixation test in 429 patients, pointing out that the test was positive in 170 of 184 patients with rheumatoid arthritis. The percentage of negative reactions was much smaller than in Singer's material. Tests made with the articular fluid of patients with rheumatoid arthritis were positive whenever the serum test was positive.

In the second part of this report, which is concerned with the L. E.-cell test, the authors point out that the clinical differentiation of rheumatoid arthritis from other collagen diseases, particularly lupus erythematosus, is frequently not sharp or clear. Joint involvement is dominant in the symptomatology of the visceral form of lupus erythematosus, and patients with rheumatoid arthritis often show the same general symptoms as do those with lupus erythematosus. The authors comment on the L. E.-cell test and cite literature reports indicating that the incidence of positive outcome of that test in patients with rheumatoid arthritis varies widely. They performed the L. E.-cell test on 100 patients, of whom 53 had rheumatoid arthritis, 4 had lupus erythematosus, and 43 were controls with various disorders. The L. E.-cell test was completely negative in 52 of the 53 patients with rheumatoid arthritis; in the remaining patient only one L. E. cell was found among several thousand cells, whereas in the 4 patients with lupus erythematosus classical L. E. cells accounted for from 1 to 10% of the cells, and, in addition, transitional cells were found. The authors feel that this difference is sufficiently sharp that there should be no differential diagnostic difficulties. In the control cases the L. E.-cell test was always negative.

PHYSIOLOGY

Does Transfusion Citrate Cause Hemorrhage? W. G. Dixon. Am. Surgeon 24:818-821 (Nov.) 1958 [Baltimore].

To ascertain whether the wound oozing that is sometimes seen after multiple transfusions is caused by excessive citrate, dogs were given rapid intravenous injections of acid-citrate-dextrose solution (which is the anticoagulant used in transfusions), and clotting times, calcium levels, tetany, pulse rates, and blood pressures were observed. Acid-citrate-dextrose solution was used instead of blood, because it eliminated the hemolytic reaction of blood itself. In addition, the smaller amount decreased the danger of overloading the dog's blood volume. The acid-citrate-dextrose solution, as prepared in Transvuso Vac blood donor bottles, contained 120 cc. of 1.37% sodium citrate, 0.5% citric acid, 2.45% dextrose, and water. This was considered equivalent to 2 Gm. of disodium citrate in calculating doses. The acid-citrate-dextrose solution was rapidly dripped intravenously either into dogs anesthetized with Nembutal, to simulate an operating-room transfusion, or into conscious dogs to simulate the patient not under an anesthetic.

In 35 experiments transfusion of acid-citrate-dextrose solution did not cause hemorrhage. Only one of the anesthetized dogs showed possible wound oozing, although the blood of almost all the dogs failed to clot as the result of so much acid-citrate-dextrose solution. Cardiac arrest occurred 26 times in anesthetized dogs and tetany 9 times in conscious dogs. The 26 cardiac arrests occurred in 11 dogs, the heart being restarted with massage 15 times. Massage might have corrected more of the arrests, except that the arrest was used to terminate most of the experiments. In 28 determinations the amount of sodium citrate to cause cardiac arrest or tetany in dogs averaged 200 mg. per kilogram of body weight, or between 10 and 20 mg. per kilogram of body weight per minute of injection.

Further Studies on Cholesterol Levels in the Johns Hopkins Medical Students: The Effect of Stress at Examination. C. B. Thomas and E. A. Murphy. J. Chron. Dis. 8:661-668 (Dec.) 1958 [St. Louis].

The authors carried out serum cholesterol determinations on 52 Johns Hopkins medical students at admission to medical school (test 1), during the final anatomy examination which is generally considered to be a severe form of stress (test 2), and during a period of regular academic work (test 3). The mean serum cholesterol levels at tests 1 and 2 were significantly higher than those at test 3. The serum cholesterol levels of 2 additional persons, who had stress studies during the biochemistry examination rather than the anatomy examination, showed a similar pattern when the values obtained during the final biochemistry examination were compared with those obtained at test 3. For certain students test 3 fell close to the final biochemistry examination; the drop in the serum cholesterol level from test 2 to test 3 was less marked in those patients. The total eosinophil count was significantly lower at test 2 than at test 3. These findings are consistent with the hypothesis that stress, such as accompanies the first few weeks of medical school or important final examinations, is accompanied by a significant rise in the serum cholesterol level.

PUBLIC HEALTH

Relationship of Amount of Cigarette Smoking to Coronary Heart Disease Mortality Rates in Men. R. W. Buechley, R. M. Drake and L. Breslow. Circulation 18:1085-1090 (Dec.) 1958 [New York].

The authors report information on cigarette smoking and data concerning coronary heart disease in 2 California population groups. The first group consisted of 3,994 longshoremen who received a multiphasic screening examination and were followed for 5 years. They were divided into 2 classes: light or nonsmokers and heavy smokers. In the first 5 years of follow-up 78 died of coronary heart disease. Of the observed deaths, 42 occurred among light or nonsmokers, compared with an expected 84 according to California age-sex-specific death rates, and 36 occurred among heavy smokers, compared with an expected 35. Similar proportions of observed to expected were not found for deaths from any heart disease other than coronary. A retrospective case-control study, by questionnaire and interview, was made in the second population group, consisting of 116 men with coronary disease and 121 matched control persons. The 116 men reported a much higher mean amount of smoking, averaging about 16 cigarettes per day, than the 121 controls who averaged about 10 cigarettes per day.

The heterogeneity of populations, differing approaches, and manner of reporting make impossible a good estimation of the magnitude of the relationship between cigarette smoking and coronary heart disease. The authors abandoned their attempts to make such an estimate from a combination of studies by various workers. However, the extent of the relationship is generally indicated by the difference in death rate between nonsmokers and heavy smokers. These differences show a strong and consistent relationship between cigarette smoking and deaths from coronary heart disease, at least in men between the ages of 40 and 70 years. The difference in mortality between cigarette smokers and nonsmokers at different ages varies from 1 to 7 excess deaths from coronary heart disease per 1,000 men per year. Smoking rates in the United States are high, and death rates among patients with coronary heart disease are also high, in comparison with many other countries. Further studies of their relationship are needed.

Bacteriology of the Bedside Carafe. C. W. Walter, A. D. Rubenstein, R. B. Kundsin and M. A. Shilkret. New England J. Med. 259:1198-1202 (Dec. 18) 1958 [Boston].

Patients' complaints of unpalatable water at the bedside called attention to the potential hazard of this water as possible vehicle in cross infection in hospitals. In 24 Boston hospitals inspectors of the Massachusetts Department of Public Health selected a carafe at random from a bedside table for the accompanying bacteriologist. Coliform organisms were found in 21.7%, and staphylococci in 68.9% of the carafes sampled. Only 5 carafes out of 103 were sterile. The tap water in the 24 hospitals contained no coliform organisms or staphylococci. Fresh Boston tap water and clean ice made from it do not support bacterial growth. Direct contamination of the water in a vessel occurs each time it is sipped through a drinking tube. The residual water in the tube at the end of the sip drains back, carrying saliva. Bacteriological contamination also occurs readily in the carafes with dual-purpose lids. Residual liquid is returned to the carafe as the cup-shaped lid is inverted. The edge of the cup also carries organisms from the patient's lips when the cup is inserted into the neck of the carafe. Grossly unhygienic conditions were described in two-thirds of the carafes. Dead, partially decomposed insects were frequently seen. The walls of some carafes were slimy; gelatinous islands of algae and fungi floated in others. Most carafes had a stale odor.

In 3 of 6 hospitals where paper cups and glasses were used instead of carafes, the water was sterile. Contamination in the other 3 was attributed to filling the cups with stagnant water from the carboy-type water cooler. The material of which carafes are made is unsuitable for sanitization by heat. Fourteen of the institutions used carafes that were destroyed by hot water at 77 C (170 F) recommended for sanitizing dishes. None of the hospitals specified the technique of the supposed daily washing of the carafes, although 9 of the 24 claimed daily washing in a mechanical dishwasher. No hospital specified disinfection as a part of cleaning. Cross contamination by faulty identification of carafes or by mixing of the lids, when several were iced simultaneously, was common. Bacteria were transferred from the fingers of personnel to the carafe in several ways. The narrow mouth of the carafe and the dual-purpose lids were often wiped with the fingers under running water as a cleaning gesture. In a third of the hospitals surveyed, the utility room was used for processing of carafes; in most of these the work was accomplished in the same area where basins, bedpans, and urinals were cleaned. In half of the hospitals the diet kitchen was used.

Ice was exposed to hospital traffic in unprotected and even bacteriologically hazardous locations. Shovels and hoes used to remove ice from machines were dirty. In many hospitals food, fruit, and beverage bottles were stored on the ice. In 6 hospitals the ice dispensers were located in utility rooms within splashing distance of the bedpan hoppers. Faulty installation and maintenance of ice makers were common. Only half of the machines were located in a protected spot.

The program recommended for providing a safe supply of bedside water includes: proper installation and operation of ice-cube makers that are isolated from sources of bacteria shed by patients and personnel; automatic bagging of ice cubes and storage at temperature less than —6 C (20 F); dispensing of ice cubes from refrigerated dispensers with ice tongs; provision of carafes with wide mouths to facilitate cleaning, inspection, and filling; daily sanitization of carafes with heat; processing of carafes in the diet kitchen by personnel trained in food handling; and complete emptying and refilling of carafes from the tap each time they are serviced. Bedside water should be of a quality comparable to the drinking water supplied the community. Where melting ice is used, it must be dispensed from a solution of sodium hypochlorite.

BOOK REVIEWS

Modern Chemotherapy of Tuberculosis. By Roger S. Mitchell, B.A., M.D., F.A.C.P., and J. Carroll Bell, B.S., M.D., M.S. Foreword by William B. Tucker, M.D. Antibiotics monographs no. 11. Under editorial direction of Henry Welch, Ph.D. and Félix Marti-Ibáñez, M.D. Cloth. $4. Pp. 109, with illustrations. Medical Encyclopedia, Inc., 30 E. 60th St., New York 22. Distributors outside U. S. A.: Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publishers, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1958.

Since streptomycin became generally available in 1947, changes in the treatment of tuberculosis have come at an accelerated pace. This monograph summarizes the present status for the physician who wants to apply the new modalities of therapy. It discusses the three principal drugs (streptomycin, *p*-aminosalicylic acid, and isoniazid) in the treatment of tuberculosis from the standpoint of dosage and duration of therapy, with an important section on mode of action and pharmacology. The principal secondary drugs are similarly but more briefly discussed. The advantages and disadvantages of single-drug and multiple-drug treatment are outlined. The net result is a perspective on the therapy of tuberculosis as a whole. With so chronic a disease as tuberculosis the final determination of the result of a particular form of treatment must wait for many years. In the meantime, decisions must be made on the best evidence available. The monograph indicates where information is not yet definitive but presumptive, and states the results of the authors' experiences. Some of their assertions may be expected to be controversial.

In a general sense, tuberculosis has come to be treated as less "chronic" and more "acute"; however, the time is not yet at hand when tuberculosis may routinely be treated in the home. Treatment is now shared by the expert with the general practitioner and internist to an extent greater than ever before. For the physician who is called on to share in this obligation, this monograph will prove valuable. The text is enhanced by an extensive and comprehensive bibliography. The chapters include history, pharmacology, modes of action, dosage, regimens, drug resistance, modern chemotherapy, diseases and conditions with adverse effect, new and less used drugs, and results of antituberculous chemotherapy to date.

Therapeutic Exercise. Edited by Sidney Licht, M.D. Third volume of Physical Medicine Library. Cloth. $16. Pp. 893, with 204 illustrations. Elizabeth Licht, Publisher, 360 Fountain St., New Haven, Conn., 1958.

This large book was written by 35 different authors (12 are European and 1 is Canadian); it has 36 chapters and two appendixes. The first 18 chapters have to do with the basic principles of therapeutic exercise such as the motor unit, physiology of exercise and fatigue, mechanical anatomy of motion and posture, and structure and motions of the shoulder, hip, feet, and hands. Several chapters discuss the various types and uses of exercise and the apparatus required, especially in hydrotherapy. There are chapters on kinetic occupational therapy, testing of muscle strength, and other tests and measurements such as measurement of articular movement. One chapter is devoted to the controversial subject of "proprioceptive facilitation in therapeutic exercise."

The last 17 chapters concern the uses of exercise in disease conditions, including scoliosis; poliomyelitis; amputations; orthopedic conditions; foot disabilities; arthritis; multiple sclerosis; paraplegia; pulmonary, heart, and vascular disease; obstetrics; and orthoptics. There is also material on exercise for normal persons and an interesting and well-documented chapter on the history of the therapeutic use of exercise. Appendix 1 is a report of a study of the effect of brief isometric contractions on muscle, as compared to the more commonly used isotonic contractions which increase strength and endurance in muscle. Appendix 2 defines the terms used in therapeutic exercise which are not fully expanded in the text.

The book has some strong chapters and, as might be expected, some that are not particularly good. The chapters on physiology and anatomy are good, but they do not integrate the material with clinical usage to any great extent. Many basic physical principles are not given. This is not really a criticism of the book, but it indicates how voluminous the subject is. Some of the chapters by authors from abroad may be difficult to follow because their approach and terminology are at variance with those in the United States. The chapter on scoliosis is especially difficult, because this is a poorly understood and controversial subject in any country or language. The chapter on postural exercise is more philosophical discussion than presentation of specific material. The chapters which discuss the disease entities or conditions are good, and, in most instances, quite exhaustive.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Therapeutic exercise implies knowledge of all motion and locomotion of the body, all basic physical and biological factors involved, and all the systems directly and indirectly related to production of energy and control. It is readily evident, therefore, that the subject cannot be adequately covered in one volume. However, as indicated by the editor, this is the largest single volume on the subject, and probably comes nearer to the goal than any other work published so far. It probably will not be used as a required text for the student of physical therapy because it is too advanced, and there is not enough material on some of the basic factors and techniques. However, it should be a valuable reference book for undergraduate students, physiatrists, and other interested physicians, and to a lesser degree for graduate physical therapists.

Sensitivity Reactions to Drugs: A Symposium Organized by the Council for International Organizations of Medical Sciences Established under the Joint Auspices of UNESCO and WHO. Edited by M. L. Rosenheim and R. Moulton. Assisted by S. Moeschlin and W. St. C. Symmers, Cloth. $7. Pp. 237, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

The symposium presented in this compact, meaty volume was organized by men from Great Britain, Belgium, France, Germany, Holland, Italy, and the United States. The 19 contributors and 5 participant observers are all investigators of one or more facets of the subject. Their fields include clinical medicine, chemistry, immunology, and hematology. In addition to a foreword and an introductory chapter, the book contains 17 chapters on hypersensitivity to drugs, each of which is followed by a discussion among the participants and a thorough list of references.

The first half of the book is devoted to discussions of changes in various blood elements (red blood cells, platelets, granulocytes, and bone marrow) due to allergic reactions caused by drugs. The last half of the book covers the following subjects: early detection of drug sensitivity; sensitivity reactions to antibiotics; nephelometric studies on the serums of patients sensitive to drugs; antibodies to drugs; the immunological character of humoral antibodies in drug allergy; chemical structure and pharmacodynamic action in relation to drug sensitivity; some general considerations on the diagnosis of the untoward effects of drugs; drug reactions linked with histamine release in man; tissue reactions produced by sensitivity to drugs; the occurrence of so-called collagen diseases systemically affecting the connective tissues, as a manifestation of sensitivity to drugs; and arteritis due to drugs. The subject index at the end is complete and accurate.

The quality of the material presented is not as variable as one might expect from the large number of participants. Most of the chapters are excellent; a few are not on a par with the others and one chapter contains conclusions based on a single case study. The discussions following each chapter are informal and at times irrelevant to the material presented. In general, this work is an excellent summary of the literature in an important and expanding field of medicine and a valuable book for the library of any physician, no matter what his field of special interest.

Economics of Mental Illness. By Rashi Fein. Joint Commission on Mental Illness and Health monograph series no. 2. Report to Staff Director, Jack R. Ewalt. Cloth. $3. Pp. 164. Basic Books, Inc., 59 Fourth Ave., New York 3, 1958.

The magnitude of the problem of mental health in terms of patients has been emphasized in recent years. In this volume the problem is approached from the standpoint of the cost of mental illness to the people of the United States—not just the expenses of hospitalization, medical care, and research, but also the money lost through the nonproductivity of the mentally ill. Admittedly, accurate figures are not available on some of these points, and estimates of such items as the amount paid in fees to general practitioners and internists by patients whose complaints are primarily psychological can be little more than speculative. It might be argued that it is not realistic to consider that all patients suffering from mental illness could be absorbed into the labor market and social order without a terrific impact on its basic structure, but recognizing these difficulties the author has attempted to present a fair estimate of the annual direct and indirect costs of mental illness which he conceives to be 3 billion dollars. The suggestion that from the economic standpoint alone it may be more profitable to increase the direct costs to provide better care and treatment for the initial admissions of the mentally ill seems logical when duration of disability is considered for patients whose illness becomes chronic. This little volume should be valuable reading for those who wish to consider not only the economic problem of the mentally ill but also the means of estimating the various factors which must be evaluated in assessing the costs of any illness.

Current Concepts of Positive Mental Health. By Marie Jahoda, Joint Commission on Mental Illness and Health monograph series no. 1. Report to Staff Director, Jack R. Ewalt. Cloth. $2.75. Pp. 136. Basic Books, Inc., 59 Fourth Ave., New York 3, 1958.

Since the Joint Commission on Mental Illness and Health was organized a few years ago under a grant of $1,500,000 from Congress, great expectations have arisen concerning its report. The Commission was designed to make a three-year study of the total mental health needs and resources of the United States and is now in its third year of operation. "Current Concepts of Positive Mental Health" represents the first phase of the total report. Approximately nine more volumes will be forthcoming, each dealing with a different aspect of the total study. The rather large sum of money to be spent in making the Commission's study, and the large number of people and organizations whose assistance was enlisted to carry it out, excited many criticisms of both its objectives and its methods. Physicians not involved in the study have frequently criticized the study on the grounds that there appeared to be a relative absence of psychiatric leadership in its actual operation. If this first monograph is representative of the entire report, this criticism will prove justified. The book consists of 119 pages of personal speculation by the author on the nature of mental health. It is a survey of a narrow segment of the literature on mental health. As the first volume of the Joint Commission's report, it is a huge disappointment. All the material presented was well known to most people in the field of mental health long before the Joint Commission began its study. The last chapter is an amendment to the report entitled "Viewpoint of a Clinician," by Walter E. Barton, M.D., a Boston psychiatrist. He takes issue with the author's view of mental health versus mental illness, but his criticism is a weak one and attacks only a minor fragment of the main issue.

Recent Advances in Cerebral Palsy. Edited by R. S. Illingworth, M.D., F.R.C.P., D.P.H., Professor of Child Health, University of Sheffield, Sheffield, England. With foreword by Norman B. Capon, M.D., F.R.C.P., F.R.C.O.G. [With appendix, Cerebral Palsy: Voluntary and Tax-supported Services in the United States, by Sherwood A. Messner, Director of Service, Medical and Scientific Department, United Cerebral Palsy Associates, Inc., of 24 pages.] Cloth. $10. Pp. 389, with 136 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, Portman Sq., London, W. 1, England, 1958.

Few subjects in medicine present as many and varied problems as does that of cerebral palsy. No one person can be an expert on all aspects of this disease; 14 specialists from the United States, England, and Australia were therefore asked to discuss the recent advances made toward meeting the total needs of the child with cerebral palsy and to decide where further investigation is needed. The result of their discussion is this authoritative treatise, which gives an accurate account of our present knowledge concerning the incidence; cause; pathology; the clinical signs by which to distinguish various types; methods of testing intelligence, speech, and hearing; drugs used in treating convulsions; and the orthopedic and neurosurgical procedures for preventing, correcting, and controlling the neuromuscular condition. There is a general agreement among the specialists that during the last decade advances have been made in these areas, but evaluating the methods of physical therapy or speech therapy is still a problem. As one author points out, it is "very difficult to determine how much of a child's apparent improvement after some months or years is due to treatment, and how much is due to the child's increased maturity." Dr. Illingsworth and his colleagues have described the recent advances in cerebral palsy and pointed out the areas which need further investigation. It behooves all those working with children with cerebral palsy to familiarize themselves with the contents of this book.

The Practice of Sanitation. By Edward Scott Hopkins, Principal Associate Engineer, Bureau Water Supply, Baltimore, and Wilmer Henry Schulze, Assistant Commissioner of Health, Sanitary Section, Baltimore City Health Department. Third edition. Cloth. $8. Pp. 487, with 141 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

This volume presents a clear, concise picture of sanitation. It is not loaded with unintelligible charts and graphs, and it covers all the significant details adequately. Any physician who may be asked about some local sanitation problem should by reading this book be able to orient himself on the matter quickly and thus be in a position to provide real help to the community. By the same token sanitarians, health officers, public health nurses, and even governmental officials who are trying to learn something about basic principles of sanitation should be helped greatly by these discussions. In this edition, the authors have wisely presented new approaches on such currently significant topics as food sanitation, air pollution, housing, rural and urban sewage disposal, stream pollution, insect control, and others of importance.

From the first chapter, in which is presented a stimulating panorama of the progress of sanitation down through the ages, to the last, which describes the establishment and accomplishment of a sanitary survey, the book is absorbing. The writing is refreshingly direct and simplified. At the end of each chapter is, in most instances, an extensive bibliography. Although not lavishly illustrated, the volume contains numerous drawings and photographs that provide additional useful information. As is pointed out in the foreword, there is no justification in this country for complacency about present sanitary practices in communities and industries. This volume provides desirable information about things that still need to be done.

The World Traveler's Medical Guide. By Richard Travis Atkins, M.D., and Jane McGlennon Atkins. Paper. $1.95. Pp. 399. Simon & Schuster, 630 Fifth Ave., Rockefeller Center, New York 20, 1958.

This volume deals with the medical aspects of travel in all parts of the world. Chapter 1 discusses medical problems related to travel by auto, train, ship, or plane; chapter 2 gives information on the required or recommended immunizations; chapter 3 furnishes useful information on such specific problems as water, milk, food, motion sickness, diarrhea, effect of altitude, and clothes to be worn; and chapter 4 discusses specific diseases and their nature. These chapters are followed by brief but adequate information as to what can be expected and what to do when confronted by a special health problem in any given country. Medical facilities in all areas, with names, addresses, and telephone numbers of English-speaking physicians, and locations of medical schools and hospitals are given. The "Guide" is unique because it deals exclusively with medical problems. According to the authors it is the first of its kind. The information given is adequate and authoritative, and the book is unhesitatingly recommended to the prospective traveler.

Physiology of Spinal Anesthesia. By Nicholas M. Greene, B.S., M.A., M.D., Professor of Anesthesiology and Lecturer in Pharmacology, Yale University School of Medicine, New Haven, Conn. With foreword by John Gillies, C.V.O., M.C., F.R.C.P.E., James Y. Simpson Reader in Anesthetics, University of Edinburgh, Edinburgh. Cloth. $6. Pp. 195, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

The author is to be congratulated for what should become a classic in the literature of anesthesiology. This book has long been needed. It discusses the physiological effects of spinal anesthesia relative to the nervous system, cardiovascular system, pulmonary ventilation and hemodynamics, adrenal functions, endocrine functions, metabolism, obstetric physiology, and gastrointestinal tract. It is well edited and printed on good paper. It is neat and concisely organized and has an extensive, carefully selected bibliography. One has a feeling that it was a labor of love which produced this truly outstanding textbook. It is strongly recommended to all individuals and libraries concerned with spinal anesthesia.

Treatment of Breast Tumors. By Robert S. Pollack, M.D., F.A.C.S., Clinical Instructor in Surgery, Stanford University School of Medicine, San Francisco. Cloth. $6. Pp. 147, with 63 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1958.

This comprehensive but brief volume is devoted to the treatment of breast tumors, including cystic mastitis. The system of classification used is simple and workable and avoids impractical detail. Diagnostic criteria are briefly discussed. The technical procedures of excisional biopsy and removal of benign tumors and other pathological processes are described. As would be expected the major portion of the book deals with various aspects of carcinoma. The importance of exploration of small tumors is stressed. The author presents his criteria for operability which are reasonably widely accepted. The practical difficulties confronting the surgeon in determining operability are well covered. Consideration is given to the indications for simple, modified radical, standard radical, and extended radical mastectomy. The procedures are illustrated. The chapters on irradiation list the indications for its use, and the methods employed are outlined. The limitations of irradiation in cancer of the breast are discussed. Additive and subtractive hormone therapy is well handled. The proper use of estrogens, androgens, and adrenocortica hormones is presented. Oophorectomy, adrenalec tomy, and hypophysectomy are evaluated as ad juncts to therapy. In controversial areas the autho presents opposing views, and an effort is made t arrive at fair and balanced conclusions. The bibli ography is extensive and up to date. The autho has presented a surprising amount of material i 142 pages. The brevity and readability of this worl recommend it as a good source of ready reference

Haematological Technique for Medical Laboratory Tech nicians and Medical Students. By E. M. Darmady, M.A M.D., F.R.C.P., Senior Pathologist, Portsmouth and Isle c Wight Area Pathological Service, Portsmouth, England, an S. G. T. Davenport, F.I.M.L.T., Chief Technician, Ports mouth and Isle of Wight Area Pathological Service. Secon edition. Cloth. $3.75. Pp. 244, with 27 illustrations. Grune Stratton, Inc., 381 Fourth Ave., New York 16; 15/16 Quee St., Mayfair, London, W. 1, England, 1958.

The authors, on the basis of practical experience describe the specific techniques for the usual bloo tests. The descriptions are adequate and are fol lowed by brief explanations of the fundamenta mechanism behind the disease process; this shoul be helpful to technicians who wish to understan the rationale of their work. In many cases, alter native methods are given. In chapter 18 a brief bu adequate account of the theory of errors in hema tological procedures and in medical statistics i given. The laboratory methods are those whic appear to be most commonly used in Britain, an the descriptions of the stained cells are based o the Romanowsky and Leishman techniques, al though the procedure for Wright's stain is als given. A short, selected bibliography follows eac section, and there is a glossary of commonly use terms. The book should prove adequate for its pur pose and should take its place among the best o the subject.

A History of Ophthalmology. By George E. Arrington Jr M.D. Foreword by Félix Martí-Ibáñez, M.D., Professor an Director of Department of History of Medicine, New Yor Medical College, Flower & Fifth Avenue Hospitals, Ne York. MD monographs on medical history number thre Under editorial direction of Félix Martí-Ibáñez, M.D. Clot $4. Pp. 174. MD Publications, Inc., 30 E. 60th St., Ne York 22, 1959.

This well-written book describes the importan events in the history of ophthalmology, not a isolated events but in relation to general historica developments. It is the author's contention tha with few notable exceptions, developments i ophthalmology are consequent to developments in religious, philosophical, ethical, and technical thought. The peculiar importance of vision in man's relationship to the external world makes such an approach particularly pertinent. Dr. Arrington states that in the past, because of this relationship, the eye was the meeting-ground of many disciplines including neurology, physiology, religion, and philosophy. In chapter 14, the author makes an almost impassioned appeal, which strikes a sympathetic note in this reviewer, that the ophthalmologist not lose himself in his techniques but view his specialty against an appropriate background of cultural knowledge. Furthermore, he emphasizes the importance of the individual in furthering the advances of the future and deplores the tendency in present society to depreciate the individual in favor of group or mass attitudes. At the end of the book are a chronological table showing advances in ophthalmology, an incomplete directory of ophthalmological periodicals, and a list of ophthalmological societies and associations. It is recommended reading for all ophthalmologists and medical historians.

Handbook of Balanced Anesthesia: Practical Techniques in Dentistry, Obstetrics and Surgery. By Sylvan M. Shane, Attending Anesthesiologist, Lutheran Hospital of Maryland, Baltimore. Cloth. $7.85. Pp. 272, with 11 illustrations. Lowry & Volz, 5701 Newbury St., Baltimore 9; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This book shows the author's tremendous enthusiasm for a specific technique and the remarkable extent of his experience with it. The book is well illustrated, neatly printed on good-quality paper, and written in a free, easy-flowing, pleasant style. However, one wonders about the title of the book, since in all fairness to the author the anesthesiologic method described is no more balanced than the thiopental–nitrous oxide–curare or narcotic–nitrous oxide–curare methods.

The author discusses clearly and concisely, with elements of enthusiasm and prejudice, his views on the methods and application of this technique in various fields. There is a rather large section pertaining to dentistry. The ancillary portion of the book is so brief as to weaken its value. It is recommended only to those who are interested in this technique, i. e., the nitrous oxide–cyclopropane–oxygen combinations in a semi-closed system. There can be little doubt that this is a vital and useful technique endorsed by the author, but the loose manner in which statements are made throughout the book would justify the use of this textbook by only those who have had large experience in anesthesiology. It is not recommended to trainees in anesthesiology–nurses or physicians. For the sake of completeness, it should be included in libraries as a reference to this specific technique.

Clinical Hæmatology in Medical Practice. By G. C. de Gruchy, M.D., F.R.A.C.P., M.R.C.P. With foreword by J. V. Dacie, Professor of Hæmatology in University of London, London. Cloth. $10. Pp. 620, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

The purpose of this book is to "bridge the gap between the inevitably short and incomplete descriptions of blood diseases found in text books of general medicine and the large comprehensive and heavily documented haematological reference books and monographs." The criticism against heavy documentation has been corrected, and the references for further reading show many contributions of British authors. The textual emphasis is on the diagnosis and clinical management of standard diseases involving the blood and blood-forming organs. Details of technique are not supplied, but enough data are given to help understand the results of laboratory examinations. Bone marrow is emphasized in connection with each disease, including photographs of tissue sections. A useful feature is a series of tables summarizing the data to be studied in investigating different diseases, or in tabulating other material of importance in connection with each syndrome (e. g., plasma clotting factors, laboratory tests in disorders of coagulation, and causes of thrombocytopenia). The book should be a useful quick reference for practitioners in the clinical management of their patients.

Clinical Neurosurgery. [Volume V] Proceedings of the Congress of Neurological Surgeons, Washington, D. C., 1957. [Robert G. Fisher, M.D., editor-in-chief.] Cloth. $8. Pp. 206, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

This volume is dedicated to Dr. Francis C. Grant of Philadelphia, who is the author of three of the papers. These papers, on gliomas in the posterior fossa in children, surgery of meningiomas at the base of the brain, and cordotomy, represent the observations of one of our most experienced neurosurgeons over a period of almost 40 years. His comments are to the point and of great value. The other papers on subdural collections of fluid in children by R. M. N. Crosby, dynamics of the cerebrospinal fluid by E. A. Bering, the treatment of hydrocephalus by shunting cerebrospinal fluid into the circulatory system by R. H. Pudenz, unilateral exophthalmos by D. D. Matson, treatment of involuntary movements by I. S. Cooper and G. J. Bravo, anesthesia for neurosurgical procedures by H. C. Slocum and H. R. Hansen, ocular signs of cerebral tumors by F. B. Walsh, and spinal nuclear amyotrophy by D. N. Buchanan are all well prepared and may be read with profit. This volume continues to maintain the high level of excellence characteristic of the four earlier ones. At the end are a list of members of the Congress and an index.

QUESTIONS AND ANSWERS

REACTIONS AFTER INJECTION OF TETANUS TOXOID

To the Editor:—*In the past year, three patients have developed delayed reactions to injections of tetanus toxoid. These reactions appeared between 5 and 10 days after the injection and were characterized by marked local redness, swelling, and itching with regional lymphadenopathy and, in at least one, some fever and polyarthritis. All subsided in one or two weeks, either spontaneously or after treatment with antihistamines and corticosteroids. They were clinically characteristic of serum sickness. The material used routinely for booster doses of tetanus toxoid is an alum-precipitated preparation produced by one of the leading biological manufacturers. Injections are withdrawn from multiple-dose vials, and other recipients of injections from the same vials have shown no reaction. The dose has been 0.5 cc. given intramuscularly (although inadvertent subcutaneous injection is possible). Careful checking makes it seem almost certain that tetanus antitoxin was not given through error, and in none of the patients was there a significant immediate reaction. Have similar delayed, presumably allergic, reactions been reported with the use of tetanus toxoid? Would a patient who had such a reaction be expected to have a similar or more severe one were he to receive tetanus toxoid at some future date?*

John E. Sweeney, M.D., Topeka, Kan.

Answer.—In the earlier period of tetanus toxoid prophylaxis, allergic reactions of variable degree were encountered. Continued efforts to use less allergenic mediums for the production of tetanus toxin, and therefore toxoid, together with techniques of purification have reduced the incidence of allergic reactions to tetanus toxoid to a statistically low figure. In the instances cited, the reactions were of the delayed serum sickness type. Presuming that no errors could be the source of difficulty (tetanus antitoxin instead of toxoid), it would be desirable to communicate with the manufacturers of the toxoid to determine the various materials used in its preparation. Sensitivity tests could be conducted with the various antecedent materials. The procedures recommended for this purpose are described in standard textbooks on allergy. In the event that the authenticity of the history, the sensitivity tests, or both indicate the existence of an altered response to one or more antecedent materials used in the preparation of the specific tetanus toxoid, avoidance of reactions at later dates could be effected by (1) avoidance of tetanus toxoid in the patients cited—periodic checks on the antibodies for tetanus could be made by collaboration with a reliable biological laboratory or by cooperation with the producer of the tetanus toxoid—and (2) use of another company's toxoid preceded by allergy tests to exclude sensitivity to the newly selected material. It is significant that a booster dose of 0.5 ml. was used in the three instances cited. In general, 0.1 ml. (injected subcutaneously, with a tuberculin syringe used for measurement and avoidance of a change of the needle used for drawing out the material from the stock bottle) is a satisfactory booster dose of tetanus toxoid (see Queries and Minor Notes, Tetanus Immunization, The Journal, April 30, 1955, page 1663).

ETHER CONVULSIONS

To the Editor:—*During operation on a 13-year-old boy under open drop anesthesia, the patient was seized with convulsions. The temperature prior to the operation was 100.5 F (38 C), and no measures were adopted to lower this temperature either preoperatively or during the operation prior to the convulsions. The patient was under light anesthesia at the onset of the convulsions, oxygen was ample, and the appendix had been uneventfully removed. Ice packs were applied. After intravenous administration of thiopental sodium, should the ether dose have been increased to reduce cerebral excitability or should the dose have been decreased because of a possible relationship to the convulsion itself?*

Norman Michael Canter, M.D., San Francisco.

Answer.—Under the conditions described, the ether dosage should not be increased nor decreased but the administration of the ether should be stopped immediately. Many theories exist to explain the cause of "ether" convulsions, but from every case described three factors emerge: (1) some form of inhalation anesthetic, usually ether, is used; (2) the temperature of the patient or his en-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

vironment is elevated; and (3) the patient has carbon dioxide retention. Knowledge of the causes of ether convulsions is still so inadequate that it is suggested that all three of these factors should be eliminated as soon as possible. With the convulsions controlled with intravenously given thiopental sodium, 100% oxygen administered, steps taken to ensure removal of excess carbon dioxide, and the patient cooled, there seems to be no good reason for giving more ether.

Ether has some unknown relationship to the convulsion, and merely to reduce the dose of ether may not eliminate whatever this relationship may be. There is no evidence that increasing the ether dosage reduces cerebral excitability in these patients. Owens and co-workers (*Anesthesiology* 18:53, 1957), using dogs with convulsions under ether anesthesia, found that increasing the depth of the anesthesia to the stage of cardiac intoxication had no effect on the abnormal electrical activity of the brain as seen on the electroencephalogram. Bowman (*Am. J. Surg.* 23:295, 1934) recorded a case in which several attempts to deepen the anesthesia in a patient with ether merely increased the severity of the convulsions. Several similar cases are recorded in the literature. Papper (*Bull. U. S. Army M. Dept.* [no. 84] p. 81, 1945) reported a case in which increasing the ether dose controlled the convulsions, but the patient was an afebrile healthy young man undergoing an elective operation. This case is atypical. The case herein described is typical in that the convulsions appeared late in the operation. If the anesthesia becomes too light to complete the operation, another small dose of thiopental sodium, and not ether, may be given. Should more muscular relaxation be necessary to complete closure of the peritoneum, a small dose of succinylcholine chloride may be used, but facilities for adequate artificial ventilation must be at hand.

HOOKWORM AND LARVA MIGRANS

To the Editor:—*Please give information on cat and dog hookworm infestation. Is this the same as larva migrans?*

Glenn T. Howard, M.D., Alice, Texas.

Answer.—Ancylostoma caninum and A. braziliense are the usual species of hookworms found in dogs and cats throughout the warm areas of the world. In northern localities in both America and Europe A. braziliense is largely replaced by A. caninum, and in Europe both species are largely replaced in dogs by Uncinaria stenocephala. Adult forms of A. caninum have been reported in man five times and A. braziliense less than 200 times. This suggests, in view of the prevalence of these two hookworms in areas where man goes barefoot, that he has a natural resistance to these two species. The larvae of these hookworms can penetrate the skin of man, but they usually go no further. The larvae of A. braziliense is largely responsible for creeping eruption or cutaneous larva migrans. The migration of these larvae intracutaneously produce serpiginous, erythematous, elevated, and sometimes vesicular lesions. The larvae migrate several centimeters a day, and the lesion extends along behind them. This migration continues from several weeks to several months until death of the larvae. The larvae of A. caninum and U. stenocephala usually do not migrate widely in the skin of man but die in the area of their original penetration, producing a localized, transient, papular eruption. The larvae of the human hookworms A. duodenale and Necator americanus and also of the nematode Strongyloides occasionally cause creeping eruption. The subcutaneous migration of fly maggots may be confused with these infections.

The existence of a large number of therapeutic agents argues against the efficacy of any of them. (Diethylcarbamazine and stibophen have been used systemically most widely, with variable success. Lowenthal (*Australian J. Dermat.* 2:171, 1954), in a statistical evaluation of chemotherapy, concluded that systemic therapy does not hasten the death of the larvae. The most satisfactory topical therapy consists in freezing the area in which the larva is currently migrating by an ethyl chloride spray. Prevention of human infection consists of avoiding skin contact with soils contaminated by dog and cat feces such as is found at bathing beaches, beneath houses, and in children's sand boxes. The latter should be covered when not in use. Hookworm-infected dogs and cats should be treated with tetrachloroethylene. Visceral larva migrans is caused by the migration through man's organs of the larvae of the dog and cat ascarides of the genus Toxocara.

ENLARGED COSTOCHONDRAL JOINTS

To the Editor:—*A biopsy specimen from a patient with enlarged costochondral joints showed normal cartilage. The joints have been infiltrated with both procaine and prednisone, with no relief. Enough pain is present so that it is hard for the patient to do his work. How can he be relieved?*

Dale R. South Jr., M.D., Troy, Ohio.

Answer.—Enlargement of the costochondral joints is usually localized to one or two ribs at the cartilaginous juncture of that rib with the sternum. No conservative plan of treatment has proved to be of any real value. Excision of the cartilaginous enlargement, together with about ½ in. of the end of the rib itself, is usually followed by complete relief. The cavity left after taking out this mass of cartilage and bone will fill with blood which will clot and organize and shortly become a firm fibrous mass which is not painful.

NICOTINIC ACID AND VISUAL SYMPTOMS

To the Editor:—*Could large doses of nicotinic acid cause an imbalance of vitamin absorption and thereby produce visual disturbance, or could such doses have a toxic effect on the retina? A 60-year-old man had, for two years, severe attacks of vertigo lasting one or two seconds and occurring every 4 to 12 weeks. Repeated physical examinations revealed no cause except the possibility of episodic cerebrovascular insufficiency, including that from stimulation of the carotid sinus. It was found, however, that the serum cholesterol level was elevated to about 265 to 300 mg.% and the fatty acid level was 584 mg.%. The elevation of the cholesterol level was confirmed on several occasions. On this basis, the patient was advised to take nicotinic acid. Small doses were given in July, 1958, and were increased to 3 Gm. daily after a few days and to 4.5 Gm. after six weeks because the serum cholesterol level remained elevated to 279 mg.%. In addition, he used a low-fat diet but consumed a liberal amount of lean meat, plenty of vegetables and fruit, and a vitamin supplement. Whatever fat was needed for cooking consisted of unsaturated fats (mostly corn oil). He lost about 7 kg. (15 lb.) in nine months and now weighs about 65 kg. (143 lb.); his height is 5 ft. 7 in. (170 cm.). On this regimen the serum cholesterol level had dropped to 221 mg.% by the middle of September and no attacks of vertigo had appeared in the preceding few months. An alarming symptom, however, had appeared: the patient, who had had myopia since youth but who had had good correction with glasses, could hardly read. He reported that print appeared "smudged." A competent ophthalmologist found that his eyegrounds were in excellent condition for a man his age and that there was no sign of glaucoma. His vision, corrected to 20/20 in each eye for years, could be corrected only to 20/30 in each eye, and the ophthalmologist found "relative central scotomata which extended about 10 degrees in both eyes." The patient stopped using nicotinic acid and took, on an empirical basis, 1,000 mcg. of vitamin B_{12} twice a week by injection and 25,000 units daily of vitamin A by mouth. On Oct. 1, the ophthalmologist found the eyegrounds normal as before. The vision, however, could be corrected to 20/20 in both eyes, and the subjective visual complaints had disappeared. Four weeks after nicotinic acid was withdrawn, the serum cholesterol level was again up to 330 mg.% in spite of the low-fat diet. Should this patient resume the use of nicotinic acid?*

Ludwig Gruenewald, M.D., Sheboygan, Wis.

Answer.—The transient "smudging" of print, some reduction in vision, and relative central scotomas do not suggest any clear-cut clinical entity, nor has an excess of nicotinic acid been reported as a cause of visual symptoms. It is suggested, therefore, that the patient's symptoms were only fortuitously related to the nicotinic acid therapy. They may have been due to circulatory disturbances of the occipital lobes. Impairment of the posterior cerebral circulation may, on rare occasions, cause central scotomas. Also, tobacco amblyopia (probably not related to nicotinic acid) may produce such symptoms as this patient had. It would be pertinent to know, therefore, if the patient smoked excessively. The foregoing case report was reviewed by a nutritionist; who pointed out that comparable amounts of nicotinic acid have been given to several hundred patients without untoward effect (Persons and others, *Circulation* 28:489, 1958, and Berge and others, *Circulation* 28:490, 1958). The doses of nicotinic acid used were, however, excessively large from a physiological point of view, and time has not permitted a definitive evaluation of such therapy. It is, therefore, important to have cases such as this on record. It may be of interest to the inquirer that there is a section in the *A. M. A. Archives of Ophthalmology* entitled Registry of Interesting Cases for the reporting of just such cases. Dr. W. B. Parsons of the Jackson Clinic, Madison, Wis., noted that visual symptoms had not occurred in 140 patients treated with nicotinic acid for hypercholesteremia except for one patient who had had transient blurring. Parsons suggested that the patient referred to in the question be treated again with nicotinic acid and control placebos to see whether the symptoms would recur.

URINE FOR CULTURE

To the Editor:—*Please supply details of a recently described method for culturing a female patient's urine which obviates the need for catheterization.*

M.D., New York.

Answer.—There are several methods of obtaining a urine culture from the female patient which obviate the need for catheterization, but none of these are practical. One such method is that of needle puncture of the bladder, using a needle introduced suprapubically into the full bladder in order to obtain a sterile specimen. This was done as a research project and would not be practical or safe for everyday use. Another technique is that of catching a mid-stream culture on a voided specimen. This is carried out as follows: The patient is given an extra amount of fluid to drink and 30 to 60 minutes later is placed on a bedpan and draped, as for sterile catheterization. The labia are then cleansed with soap and water, benzalkonium chloride, and dry sponges in succession, and this procedure is repeated three times to completely clean the vulva and urethral meatus. During this time, the labia are held apart to expose the urethral meatus and must continue to be held apart during the preparation and the voiding. After preparation, the patient is asked to void and the urine is caught during mid-stream in a sterile test tube. This technique also has the disadvantages that it requires elaborate preparation, may be embarrassing for the patient, and does not eliminate the possibility of contamination.

Clabaugh and Rhoads (*J. A. M. A.* 165:815-818 [Oct. 19] 1957) described a technique of catheterization which avoids the possibility of introducing bacteria into the bladder and also of false contamination of the catheterized specimen. This technique uses a large catheter which is advanced part way into the urethra, almost to the bladder neck, followed by a smaller catheter introduced within the large catheter and advanced completely into the bladder to obtain the specimen. This does away with any possible urethral contamination by the actual catheterizing tube. It is, however, cumbersome in the hands of ordinary hospital nurses. Recent studies indicating the frequency of bacterial contamination of the urinary tract from catheterization have led many physicians to fear catheterization and to avoid it when at all possible. This consultant believes that a properly conducted catheterization is not dangerous, and one should not hesitate to perform catheterization when there are specific indications for doing so.

PAINFUL CORNS

To the Editor:—*An item in* Science News Letter *(Jan. 4, 1958) states that injections of vitamin A palmitate under painful corns have been able to stop pain. Is this treatment recommended?*

M.D., Louisiana.

Answer.—The injection of an aqueous solution of synthetic vitamin A palmitate under painful corns cannot be recommended. Drummer, the podiatrist whose work was noted in the *Science News Letter*, wrote in the March, 1958, issue of the *Journal of the American Podiatry Association:* "Naturally no heloma [corn] can be permanently cured unless the cause is removed." The causative factor in most corns is enlargement of the head or base of one of the phalanges of the toe. Dr. Drummer, in his series of 21 cases, injected a local anesthetic into the site before injecting the vitamin A. Over the years, similar results have been obtained by injecting sclerosing materials, local anesthetics, corticosteroids, or sterile water into the area. In the September, 1958, issue of the *Journal of the American Podiatry Association*, Levy reported a controlled evaluation of the subdermal injection of corticosteroids. In his series, he found that 58.6% of the patients received relief from pain with no side-effects when he injected only the vehicle in which the corticosteroids were suspended. This compared with 42% of the patients receiving relief from pain, with side-effects in many cases, when the corticosteroids were given. He further stated: "There is some question whether the corticosteroids have produced any therapeutic effect that would not have been produced by supportive measures and the injection of the control solution." The only way to relieve pain from a corn is to remove the cause, use protective padding, and wear proper footgear.

Answer.—Vitamin A palmitate has been used in a few patients and results have been considered good, but this consultant cannot state definitely that these results were entirely due to the injections of this compound, because electrocoagulation was used as an adjunct. Simple injections of local anesthetic agents beneath the growth, followed by electrocoagulation, have also been used, and in some instances the results were about as good as with the use of vitamin A. It appears that the resultant damage to the growth can be accomplished by some simple injections of other chemicals in a similar manner.

EPINEPHRINE

To the Editor:—*A man in his fifth decade was recently treated for hives, with 0.3 cc. of a 1:1,000 solution of epinephrine subcutaneously, with no apparent effect. A few days later he was given 0.42 cc., again without effect. At this time the manufacturer replaced the supply of this agent with new stock. (The old stock was subsequently tested on another patient and was found to be potent.) On his third visit, the patient was given 0.6 cc. of epinephrine at 9:30 a. m. His pulse rate was 84 per minute before the administration and remained stable. At 10:00 a. m. he was given 0.45 cc. of epinephrine, followed in two minutes by another 0.45 cc. minims. He was observed closely for 30 minutes. There was no evidence of flushing, tremor, or increase in pulse. At 11:15 a. m., his pulse rate was 88 per minute and he had experienced no noticeable effects from the injection. The urticaria at this time had receded but was still visible. The patient gave the history of having taken 100 mg. of ACTH per day for several days in 1950 for iritis. Prior to the present illness, he had never been given epinephrine. Is this experience unusual? What is the connection, if any, between previous large doses of ACTH and refractoriness to epinephrine?* *James N. Dewane, M.D., Chicago*

Answer.—The injection of 0.5 to 1 mg. of epinephrine in normal persons is usually followed by a rise in systolic blood pressure, a fall in diastolic blood pressure, a rise in pulse rate, and, frequently, subjective feelings of anxiety; however, there are wide individual variations. In some persons no response occurs, while in others the response may reach alarming proportions. The differences undoubtedly depend to a large extent on the rate of absorption of the drug. This tends to be slow, due to the local vasoconstricting action of the drug; subcutaneous injections are more slowly and erratically absorbed than intramuscular injections. Therefore, while patients with certain conditions, such as myxedema, are said to be characterized by a relative tolerance to epinephrine, the normal variations are so wide that interpretation of the response under abnormal conditions is difficult. There is no reason to believe, however, that the previous large doses of ACTH could have influenced the response of the patient to epinephrine.

DEATHS DUE TO TETANUS ANTITOXIN

To the Editor:—*Please give statistics on the annual number of deaths caused by giving tetanus antitoxin. How many deaths occur annually from tetanus? Is it not true that many physicians refrain from giving tetanus antitoxin unless the injury occurs in a barn or other place where the chances of tetanus are great?*

M.D., California.

Answer.—Deaths from tetanus antitoxin administration are not tabulated as such but are included in the International Classification of Diseases, Injuries and Causes of Death under E 944—other complications of prophylactic inoculation. This title includes reactions and complications resulting from inoculation of a biological substance, including immune serum, for immunization or other prophylactic but not therapeutic purpose. It does not include reactions and complications after vaccination against smallpox and postimmunization jaundice and hepatitis. The published figures of deaths in this group are low—4 deaths in 1956, 14 in 1955, and 10 in 1954. According to the National Office of Vital Statistics, the deaths from tetanus for the period of 1952-1956 are as follows: 1952, 360; 1953, 337; 1954, 332; 1955, 265; and 1956, 246. These figures include tetanus neonatorum but exclude puerperal tetanus. In the absence of previous active immunization with tetanus toxoid, antitoxin should be given after injury in all instances where contaminated material may be imbedded in a wound. To confine such practice only when the injury "occurs in a barn" seems a rather hazardous procedure; Clostridium tetani has consistently been found not only in manured soil but also in street dust and, exceptionally, even in the dust of hospital operating rooms. The injection of antitoxin should be followed, in the next few weeks, by a full course of active immunization with toxoid, since tetanus might not develop for weeks or months after the wound has healed. If adequate immunization has been done four or five years before the injury, a more effective method of prevention consists in giving a booster injection of fluid toxoid within a few hours after the wound occurs.

PAROXYSMAL TACHYCARDIA

To the Editor:—*In a known case of paroxysmal auricular tachycardia, 20 cc. of 10% calcium gluconate was given intravenously with apparently prompt restoration to a normal sinus rhythm. If this should fail, would it be permissible to follow this promptly with an intravenous digitalizing dose of lanatoside C?*

Glenn T. Howard, M.D., Alice, Texas.

Answer.—There is experimental as well as clinical evidence that intravenous injection of calcium salts per se may precipitate as well as abolish arrhythmias due to ectopic impulse formation and may also suppress the activity of the primary pacemaker and cause cardiac arrest. Furthermore, cases are on record in which sudden death was ascribed to intravenous injection of calcium after digitalization. Although a potentiating effect of calcium and digitalis, suggested by these observations, has not yet been definitely established, the use of the two drugs in conjunction or in short succession seems to be associated with a great risk and should, therefore, be avoided.

HYPNOSIS MACHINE

To the Editor:—*It is said that a brain wave synchronizing machine, that will induce hypnosis, is available to the medical profession. Since the American Medical Association has accepted hypnosis, properly controlled, please comment on the use of this machine, especially in obstetrics.*

M.D., California.

Answer.—The brain wave synchronizer is an electronic instrument designed to induce various levels of hypnosis by subliminal and photic stimulation of the brain waves. The inventors, a clinician and an engineer, have developed a method for "driving" the alpha rhythm. The instrument can be used alone or combined with a tape recording of the therapist's induction and dehypnotization techniques. Easily followed directions enable proper use of the apparatus. The instrument definitely increases receptivity to suggestion and has been clinically tested on more than 2,500 subjects, including over 200 obstetric patients attending group hypnosis prenatal training classes. The apparatus induced light to deep hypnotic levels in over 90% of the subjects. Hypnotic response is more readily produced if a favorable "mental set" is created. Therefore, to some extent, the expectant attitude created by the structured situation enhances the hypnotic response, but about 30% of the subjects who had received no explanation or verbalization and who had no knowledge of what the brain wave synchronizer would do were hypnotized to various degrees ranging from light to deep states. The apparatus has remarkable potentialities for deepening a previously fixed hypnotic level and for facilitating and speeding up hypnotic induction, which often can be time-consuming, especially in refractory subjects. It also can help make labor and delivery a more gratifying experience by reducing discomfort and the need for excessive analgesia and anesthesia. Thus, the brain wave synchronizer has wide application to clinical and experimental hypnosis research. A distinct advantage is that no physical connections or attachments are placed on the patient. The unit weighs only 7 lb. A detailed scientific report will appear in the April 1959 issue of *The Journal of Clinical and Experimental Hypnosis.*

TETANUS AND DOG BITES

To the Editor:—*Since the tetanus bacillus is an anaerobe, is it possible that tetanus can be transmitted from a dog bite? In this locality, a number of physicians give antitetanic serum to all patients bitten by a dog. Would a physician be liable for a malpractice charge for omitting the immunization if, subsequent to a dog bite, a patient should develop tetanus due to a minor injury which may have escaped the patient's attention?* *M.D., California.*

Answer.—Reference is made to questions that have previously appeared in this section: "Tetanus After Human or Dog Bites" (*J. A. M. A.* 16:1445 [Aug. 16] 1947), "Human Bites" (*J. A. M. A.* 156:1297 [Nov. 27] 1954), and "Tetanus Protection Following Dog Bite" (*J. A. M. A.* 166:429 [Jan. 25] 1958). A clean dog bite would not require protection of the patient against tetanus. A bite contaminated with dirt would validate specific prophylaxis (tetanus toxoid, tetanus antitoxin, or both, as indicated). Spaeth (*Nebraska M. J.* 41:224, 1956) gives indications for these. In general, the literature on tetanus makes no specific reference to the disease after dog bites. If tetanus should develop later from some other minor, undetected injury, it is not likely that the physician would be held guilty of neglect. However, to preclude such a situation, it would be desirable to inject a booster dose of tetanus toxoid provided (1) adequate basal protection with tetanus toxoid exists, (2) a booster dose has not been given recently, and (3) there is no epidemic of poliomyelitis (danger of paralytogenic effect of an injection if undetected viremia with poliomyelitis virus exists). In the absence of a significantly contaminated wound, if basal immunity against tetanus does not exist, tetanus antitoxin with its multiple potential complications would not be indicated. The general trend of thought among physicians responsible for the treatment of dog bites has been to avoid antitetanic serum in the presence of dog bites. Major emphasis has been directed to the prevention of rabies.

PSORIASIS

To the Editor:—*A 76-year-old patient developed about a dozen lesions on his legs and a fine rash on his hands which, though it could hardly be seen, could be felt. All the lesions itched intensely. When the condition was definitely diagnosed as psoriasis, triamcinolone was given and there was an immediate improvement, with the rash on the hands completely disappearing. The dosage of 4 mg. four times daily was gradually reduced to 2 mg. twice daily. Is there any reason why the present dosage should not be continued, and is there a prospect of the patient getting perfectly well?*

Howard M. Cooper, M.D., Rutherford, N. J.

Answer.—There is no very satisfactory treatment for psoriasis, nor can one give a prognosis with any certainty. Psoriasis may occur at any age. The course of the condition may be brief or last for many years. Therapeutic measures, intelligently used, often minimize the problem. Among topical remedies, the tars, ammoniated mercury, and such keratolytic agents as salicylic acid in various combinations have stood the test of time. Ultraviolet light may also have a beneficial effect in some cases. The use of steroids, such as triamcinolone, should be reserved for so-called psoriatic cripples and should be used for short periods only, for the steroids are not curative—they merely serve to control the acuteness of the lesions. Prolonged use of these drugs is attended by well-known risks, which hardly seems justified for a condition of no greater severity than the one described.

PREGNANCY AND LUPUS ERYTHEMATOSUS

To the Editor:—*A patient in her last trimester of pregnancy has had serious recurrent attacks of generalized lupus erythematosus. During the last acute exacerbation six months ago, she received large doses of prednisone; this dosage has gradually been reduced. She has had no cortisone derivative for the past two months, and her condition is fairly good, with no specific symptoms or complaints. What can be expected during and after delivery? Will there be any effects on the baby?* *M.D., Montana.*

Answer.—In all probability, the delivery will proceed normally. According to Haserick (*A. M. A. Arch. Dermat. & Syph.* 75:706, 1957), there were seven normal deliveries in eight pregnancies in a group of 165 patients with systemic lupus erythematosus. This is in contrast to the presteroid era reported on by Ellis and Bereston (*A. M. A. Arch. Dermat. & Syph.* 65:170, 1952), in which there was a 30% fetal mortality. The child should be normal, since systemic lupus erythematosus is not a familial or congenital disease. The prednisone administered early in the pregnancy or just prior to its inception should not prove deleterious to the infant. There is a difference of opinion among dermatologists as to the future care of such patients. The mother should be given clinical and laboratory surveillance. Friedman and Rutherford (*Obst. & Gynec.* 8:601, 1956) stated that the disease often improves during pregnancy but reverts to its prepregnancy state usually within two months post partum. If the patient remains afebrile and clinically well after gestation and there is no laboratory evidence of activity, active treatment should be withheld. Corticosteroid therapy is of suppressive value only, and therefore its use should be reserved for the treatment of signs and symptoms of this disease. It is doubtful if there is any logic in treating subclinical systemic lupus erythematosus as one would treat latent syphilis. Avoidance of sunshine, adequate rest, and maintenance of strength and weight should be recommended.

TUBERCULOSIS CONTROL

To the Editor:—*A question has arisen in connection with a revision of the tuberculosis control program in Wyoming. It is planned to abandon a sanatorium located in an isolated area and to build, in effect, another sanatorium in a city for the care of patients with tuberculosis. It has seemed that the current trends in therapy were in the direction of treating tuberculous patients in general hospitals near their homes rather than grouping them together in a location necessitating a separation from their families. Have the newer trends in therapy changed the thinking on this score? Can any qualified chest surgeon perform the required operations, or is this a more narrowly specialized field?*

Lloyd R. Evans, M.D., Laramie, Wyo.

Answer.—The trend in the United States is against the care of patients with tuberculosis in isolated institutions and toward urban locations for tuberculosis hospitals. Many general hospitals operated by larger counties have tuberculosis units for the care of residents of those counties. The same is true of hospitals operated by large cities. Proximity to general hospitals is essential for the provision of all special services, especially thoracic surgery. The sanatorium concept has given way to the hospital concept in the care of such patients. The new therapies have brought this about. Conversion of sputum occurs sooner, operations are performed often and early, and the duration of the patients' stay is lessened. Not many private general hospitals provide a tuberculosis unit or even welcome individual patients for long-term care. While desirable, this development still lies in the future. In general, chest surgery is done by thoracic sur geons, and their services are available in practicall all centers of population, not merely the large centers. Some general surgeons have had trainin in thoracic surgery and are competent in this field

GRANULOMA ANNULARE

To the Editor:—*A 13-year-old boy has typic granuloma annulare lesions on the dorsum of h right hand. This has been unsuccessfully treate with ultraviolet light. There has been a hesitatio to recommend radiation for this so-called benig lesion. Would streptomycin be of benefit? Wh other methods of approach are there to th problem?*

David K. Wagner, M.D., Santa Fe, N. Mex.

Answer.—Granuloma annulare is a capricio entity responding to different modalities in differe cases. Streptomycin may or may not be effectiv but its toxicity is much greater than that of x-radi tion and it is also more unpredictable. Such a dr should be used as a last resort. The first thing to is to examine a biopsy specimen. This procedu would confirm or disprove the diagnosis, since t histopathological architecture of this dermatosis characteristic. This maneuver is followed in ma instances by disappearance of the lesions of gran loma annulare. If this should fail, x-ray thera would be recommended. In the dosage and qua ties, with proper shielding, used by the derm tologist, the radiation does not damage the ski shorten life, or cause leukemia or genetic mut tions. However, if the physician or the patient st fears this modality, freezing with solid carb dioxide or carbon dioxide "slush" would be reco mended. There is no end of other methods th have been suggested, including the subcutaneo injection of hydrocortisone, intramuscular injectio of bismuth subsalicylate, and use of antimalar drugs, sulfonamides, and ultraviolet light.

URETERAL OBSTRUCTION

To the Editor:—*What happens to the human ki ney if a ureter is tied off?*

Len H. Andrus, M.D., King City, Calif.

Answer.—If a ureter is tied off, the kidney pr tically always becomes hydronephrotic and pain in varying degrees. Perhaps half of such kidne become infected, requiring subsequent surgical tention. At times, the pain in the tied-off kidn is not pinpointed in the postoperative recove period but disappears, only to recur when uri begins to trickle through the ligated ureter and t kidney begins to function partially. If both uret are inadvertently tied off, the absence of urine i tiates an immediate investigation usually resu ing in fairly rapid deligation of the ureters.

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PREVENTION OF INJURIES IN COLLEGE ATHLETICS

Augustus Thorndike, M.D., Cambridge, Mass.

The records of 14,375 contestants in organized college athletics over a period of 17 years, embracing 36,050,885 practice-periods or games, showed 3,453 injuries severe enough to exclude the player from one or more subsequent practice or game sessions. This high incidence of 24% indicates the need for insisting on the player's "bill of rights" which is here stated. It includes good coaching, good equipment, and good medical care. The medical care includes a thorough preseason examination, the presence of a physician on the playing field, and due respect for his authority. A case history illustrates the prolonged disability and permanent residual damage done by ill-advised treatment of athletic injuries. Responsibility for diagnosis and treatment of athletic injuries should not be imposed on coaches and trainers but assumed and duly discharged by the physician.

THERE APPEARS to be general agreement that the incidence of injury in the United States is too high. Industry has reduced the incidence of industrial accidents markedly by a continuing educational and training program among its plant supervisors. Highway safety engineers have so far been unsuccessful in reducing the accident and death rate among our motoring public. The true incidence of sports injuries is not known for lack of accurate statistical data. Were this incidence known, something would be done about making our athletes, our coaches, trainers, and team physicians, the sports rules committees, and the sports equipment manufacturers more conscious of their responsibility in providing more safety measures. Our experience with the incidence of sports injuries is presented in table 1.[1]

In a period of 22 years this demonstrates the great increase in sports participation at our college. Considering that the intramural program this winter included 52 hockey games, 113 basketball games, and 152 squash racquet team matches, one realizes that student participation in exercise activities is high. In all sports this program averages 2,400 individual students, more than 50% of college enrollment. In varsity, junior varsity, and freshman sports, an estimated additional 1,700 of the college enrollment should be included. In other words, about 76% of our college student body is participating in organized sports.

In table 2 an attempt has been made to analyze the incidence of injury in 17 academic years (fall of 1936 through spring of 1954) by the number of exposures (practice or game sessions). I am not cer-

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Chief of Surgery, University Health Services, Harvard University, and Lecturer on Surgery, Harvard Medical School.

Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

tain just what one can derive from this computation. In recording injuries, only those injuries are recorded that prevent a player from participating in one or more practice or game sessions. However, 3,453 injuries among 14,375 contestants represents a high incidence, namely 24%.

Table 1.—*Total Number of Athletes in Organized Sports in Harvard College from Fall, 1932, to Spring, 1954*

Season	1932-1937	1937-1912	1942-1947	1947-1954*	Totals
Fall	3,271	2,477	703	6,485	12,936
Winter†	1,235	1,662	280	8,895	12,072
Spring	2,112	2,720	445	7,670	12,947
Total	6,618	6,859	1,428	23,050	37,955

*The last period is for seven academic years rather than five. Since 1947-1948 the varsity and junior varsity football participants have been averaged.

†The figures for winter sports include only hockey and winter track, the only major sports in that season until 1937, when swimming and basketball were made major sports.

Any program for prevention starts with the individual player, who is entitled to his "Bill of Rights."[2] These are as follows:

(1) Good Coaching. This has practically been realized. The coach who teaches unsportsmanlike tactics to win at any price is almost extinct. Almost all coaches today are competent instructors in the technical aspects of the game, ignorance of which greatly increases the incidence and severity of injuries.

(2) Good Equipment. This, too, can easily be achieved. The equipment manufacturers take their responsibilities very seriously and are continually modifying and improving the various types of armor worn in contact sport. The problem lies in the false economy of using worn out, outmoded, or ill-fitting gear. The outfitting of a team is no place for penny pinching.

(3) Good Medical Care—which has three aspects:

First—a thorough preseason history and physical examination. This is the most important single factor in the prevention of injuries. A considerable number of the tragedies which occur every year are due to medical conditions such as heart disease, hypertension, and diabetes which were not recognized and usually constitute contraindications to participation in contact sport. For many years at Harvard, loss of function of any of one paired set of organs has also been regarded as contraindication for participation in body contact sports. This rule produces an annual crop of unhappy young men who seem to have played for years in high school with one testis, kidney, or eye, but we have made no exceptions. Other less potentially dangerous sports are available, and no game is worth the risk of blindness, death, or castration.

Another important aspect of the preseason examination, particularly in high schools and preparatory schools, is the proper matching of players. Boys grow at different rates. Some at 15 have mature and well-coordinated musculoskeletal systems. Others are small and soft, having barely entered the wondrous years of adolescence, and still others are large-boned, skinny, and uncoordinated, being in a period of rapid bone growth, with barely compensated nerves and muscles.

To mix these types on a team is to look for trouble. This is an area for cooperation between coach and doctor. Well-matched teams are much safer and much more fun for all concerned.

Second—A doctor should be present on the playing field at every scrimmage and game. To leave to a trainer or coach such decisions as whether an injured player should continue play or be removed, whether he should be carried or walk off the field is to gamble with the player's future with the cards stacked against him.

Third—A doctor's authority in matters medical should be absolute and unquestioned. This principle is the measure of a good coach. Almost all coaches today are happy to leave medical decisions to the medical profession. They have enough difficult decisions and problems as it is.

Granted that this "bill of rights" has been fulfilled, injuries will still occur. Fortunately the very great majority are minor, and fall into the category of contusions, strains, and sprains.

With this "bill of rights" understood by coach, trainer, doctor, and player, each must play his part in coordinating the measures required to minimize the injuries. In contact sports the teaching of special techniques and the timing in coordinated team play are factors often not understood by the casual observer. It requires long hours of practice to develop timing in a team, and this is practice in live scrimmage. The doctor and trainer must be trained to observe and detect a "limping" or a "groggy" player from some yards distance. Continued play on a minor sprained ankle can aggravate a grade 1 lesion and often may result in an unnecessarily prolonged disability period. Each day of disability is a day lost not only in the player's development but also in the squad or team development. From our experience recurrent sprains can be controlled by protective adhesive strapping daily, plus a progressive resistance exercise program to the muscles in and about that joint. This is essentially controlled under the direction of doctor and trainer for the benefit of the player.

Preseason conditioning exercise to develop muscle tone on schedule is absolutely necessary. Within the last few months Professor Emeritus McCloy of the State University of Iowa has prepared and published a program for the National Federation of High School Athletic Associations which has been distributed to the members of this association. The exercise program is clearly defined and illustrated and can be followed by each preseason candidate at home. This is a great step forward, and if carried out in our high schools and colleges should have a significant influence on the early season injury incidence. Not only sprains but muscle or tendon strains are the bugbear of coaches and doctors in early season practice. Such can be prevented by the players returning for the first session of practice preconditioned.

Table 2.—*Total Contestants and Total Injuries as Related to Total Exposures**

Sport	No. Out†	No. of Exposures‡	No. of Injuries
Fall	3,840	3,741,477	2,170
Winter	4,268	13,989,276	470
Spring	6,267	18,320,132	813
All	14,375	36,050,885	3,453

*Exclusive of intramural teams, fall, 1936-spring, 1954, inclusive; and excluding the years, fall, 1942-spring, 1946, for which complete figures are unavailable. Since 1947-1948 the varsity and junior varsity football figures have been averaged. Data from Thorndike,[1] p. 66.

†The figure in the "No. Out" column represents the average of men out in each sport each day.

‡An "exposure" is taken to mean one afternoon period of practice or play for each man in each sport.

Another item that contributes to injury incidence is the player's apathetic attitude toward proper adjustment of pads. It is not uncommon to find football players who neglect to tighten or lace their shoulder pads or underarm elastic webbing straps. Furthermore, many of us have seen hip pads worn that are inadequate protection in order that the player in his own thinking might gain running speed. The proper wearing of protective equipment is the responsibility of coach, trainer, doctor, and player.

In the wide expanse of playing fields at Harvard, during the fall season, my staff consists of four surgeons and four trainers on the fields when contact sports are taking place. Through the week, one additional surgeon is in the field house clinic each afternoon and on Saturday one surgeon with each competing team other than with varsity football.

In order that the incidence of injury in organized athletics may be better known, it behooves those of us working with athletic trauma to report our results on a wide-scale basis. What is the true incidence in football, at the college level or at the high school level? Before one can determine such, one must have accurate records of diagnosis and period of disability of each injury on each college or high school squad, and until such a record is obtainable from the colleges and schools one hesitates to even hazard a guess. One fact is certain; namely, this incidence is too high, and the disability period in most instances is too long. From the coaches' point of view every day lost from practice not only hurts the player and his normal development in newly learned techniques but also hinders the whole squad's development.

In the past, several groups of interested associations have tried by questionnaires to obtain information on the incidence of injuries in sport, but the replies received were so few that the attempt at recording was abandoned. A recent study of this situation concerned all trauma on college campuses undertaken by the American College Health Association and the National Safety Council over a two-year period.[3] The first year 11 colleges participated, the second year 9. The report did not separate purely athletic trauma from other types, so that it failed to reveal anything on the incidence of trauma from sports. The National Federation of High School Athletic Associations is now embarking on a new attempt. One may rightly inquire as to where such a collection of data should be centered. To my mind, either the National Collegiate Athletic Association and the National Federation of High School Athletic Associations or the National Safety Council and the American College Health Association should be the source of such an annual report.

But can all colleges or schools render an accurate report of all athletic injuries? To obtain the complete picture of athletic trauma and its true incidence, it must cover all sports which are in intercollegiate and interscholastic competition. The records analyzed should be medical in origin and include at least an accurate medical diagnosis and the disability time lost from the squad season. With this material available from a good sample of schools and colleges, one can then draw significant conclusions. It can be undertaken regionally or nationally. Let us make a start toward accurately determining the true incidence of athletic trauma.

What measures can be taken to lessen the incidence of injury? Development of the rules of the sport, and the enforcement of these rules by the officials, is one item that has altered the incidence of injury. The protective equipment (padding) and its design is another. Just now we are looking for a better football helmet, and we think we have it, but the manufacturer can supply it in only one size. The design and construction of some pads afford little if any protection to the wearer. New materials are being tried in the fabrication of pads that have been inadequately tested in the laboratory and on the field. The third item, proved to reduce recurrent ligament sprains, is proper protective adhesive strapping for every practice or game. It matters significantly whether ligaments had been sprained in high school prior to entrance to college, and in such instances they receive daily strapping from the start of the season.

The purely medical prerogative is the diagnosis, treatment, and prognosis of all individual injuries once sustained. In addition, the prerogative pertaining to the prevention or aggravation of minor injury belongs to the medical staff. No one can deny that progress has been made in reducing the days of disability from athletic injuries. Table 3 demonstrates significantly the results of early, prompt treatment. Physicians, trainers, and coaches are all concerned with the individual player and his welfare. The permitting of a player with cerebral concussion to continue play should not be tolerated. Even the player who is exhausted physically and physiologically is more prone to injury if permitted to continue.

TABLE 3.—*Incidence of Sprains and Length of Disability Incurred in Sports at Harvard University*[*]

	Ankle Sprains, No.		Disability Days		Knee Sprains, No.		Disability Days	
Sport	1946-1947	1953-1954	1946-1947	1953-1954	1946-1947	1953-1954	1946-1947	1953-1954
Varsity football	7	2	55	35	4	5	34	46
Jr. varsity football	7	3	96	15	5	4	71	41
Intramural football	12	1	75	30	9	3	139	58
Totals	26	6	226	80	18	12	244	145
Av.			8.69	13.33			13.56	12.08

[*] From Thorndike, A.: J. A. M. A. 162:1126 (Nov. 17) 1956.

A player not mentally or physically capable of carrying out his assignments is of less value to a team than a fresh substitute. Every follower of body-contact sports can recall having seen some player allowed to continue in a rugged contest without full capacity of his mental processes. In the high school leagues, particularly, there is lack of adequate medical supervision of practice sessions of contact sports. The responsibility lies in the community schools' committees.

According to Eastwood's report[4] of the nine football fatalities in 1955 that were a direct result of competition, six were deaths of high school players. It is unfair to a coach not to provide him with adequate medical assistance. Even though the majority of injuries sustained are not serious, nobody can prophesy when a serious accident might occur.

The team physician must grasp the opportunity to determine whether a limping player should be taken out of competition. He should arrange with the team captain to call time out for any needed examination. He should be familiar with the functional testing of joints, the more common sites of fracture, and the simpler tests for diagnosis of type of injury. In instances of head injury, he should be alert and ask the player simple questions in order to determine whether there is amnesia with loss of orientation of time and place. If necessary the physician could call on the team captain to interrogate the injured player in order to determine whether the player knew his particular assignment in an individual play signal. When an arm or leg is involved, comparative tests of the normal side and the injured side are simple and practical.

TABLE 4.—*Types of Injuries Incurred Most Commonly in Sports at Harvard University**

Injury	1932-1937	1937-1942	1942-1947†	1947-1952	1952-1954	Totals
Sprains	636	426	210	344	86	1,702
Strains	363	287	96	145	53	944
Contusions, joint	219	73	87	52	17	448
Contusions, muscle	526	350	111	60	18	1,065
Contusions, simple	281	93	103	97	22	596
Fractures and dislocations	223	232	105	181	47	788
Lacerations and abrasions	264	89	25	40	6	424
Inflammations and infections	300	131	66	48	9	554
Internal injuries	102	81	39	115	26	363
Miscellaneous	243	152	67	42	6	510
Totals	3,157	1,914	909	1,124	290	7,394

* Data from Thorndike,[1] p. 66.
† From fall, 1943, until spring, 1946, sports were on a wartime basis, with organized sports continued only informally and on a limited basis.

Once the injury is located and diagnosed, its severity or degree is the important decision to make. Will continued play turn a sprain from grade 1 into grade 2 or grade 3? In many instances one cannot determine the degree of injury until 24 hours later. The player should be protected from an unnecessarily long disability period. There is no reason, from a pathological point of view, to think that an acutely sprained ligament can be supported by adhesive strapping, so that the player can be returned immediately to play without doing irreparable harm to the injured ligament. The torn ligament must heal, and one cannot put stress on it until the healing process is complete, and then only with daily supportive adhesive strapping. It will never again be as strong, since there will be fibrous scarring. The too early return to play of a player with a healing sprained ligament can undo good results of the partial healing process. The team physician must determine when the lesion has healed and the player is ready to return to play. He must realize that, if a player still limps, an ankle sprain is incompletely healed and that, regardless of the amount of adhesive tape applied, the player cannot yet withstand the stress of running and dodging.

The team physician must become familiar with the more common types of injuries produced in athletics and likewise the more commonly injured parts of the body. Tables 4 and 5 illustrate my own experience. Alertness on the part of the trainer and team physician and recognition of the more serious and less common injuries is a "must" in organized sports. In most body-contact sports, there is a time limit of three minutes in which the one responsible for diagnosis and prognosis must decide whether an injury is of sufficient degree to require the player to leave the field.

In view of the fact that many injuries in contact sports are recurrences of prior injuries, one must emphasize the importance of proper preventive measures to reduce the incidence of recurrent injuries. It should be noted that the use of procaine (Novocain) hydrochloride or some of its derivative with hydrocortisone and hyaluronidase has been known to cause complications. I wish to cite a case from the records of Dr. Carl Badgley, professor emeritus of orthopedic surgery, University of Michigan, Ann Arbor.

TABLE 5.—*Body Distribution of Injuries Incurred in Sports at Harvard University**

Region	1932-1937	1937-1942	1942-1947	1947-1954†	Totals
Abdomen	18	10	1	8	37
Achilles tendon	31	5	3	4	43
Ankles	344	200	125	226	895
Arms	38	35	12	15	100
Back	87	57	5	32	181
Buttocks	29	10	0	3	42
Calves	147	91	48	14	300
Chest	75	48	55	35	213
Crotch	27	0	0	1	28
Elbows	53	38	21	12	124
Face	228	122	44	48	442
Feet	187	68	39	45	339
Groins	114	108	39	21	282
Hands	288	109	55	41	493
Head	182	109	71	140	502
Heels	32	8	2	3	45
Hips	58	26	0	4	88
Knees	426	301	137	273	1,137
Iliac crest	30	29	24	28	111
Neck	20	14	1	11	46
Shins	54	16	7	60	137
Shoulders	212	189	64	129	594
Teeth	14	1	0	11	26
Thighs	416	240	113	142	911
Throat	11	6	6	15	38
Viscera	35	42	16	12	105
Wrists	51	32	21	31	135
Totals	3,207	1,914	909	1,364	7,394

* From Thorndike,[1] p. 137.
† For seven academic years rather than five.

This 19-year-old college football player was first seen July 29, 1957, for painful swelling below the medial malleolus of his right foot. He was seen in consultation at the request of the boy's father. The doctors at the college had placed his leg in a plaster cast for one month four months previously; after removal of the cast there was considerable improvement in function of the leg, without pain. However, on resuming physical activity he had a recurrence of symptoms. Physical examination revealed ½ in. atrophy of the right calf and locally there was definite thickening of the tissues about the posterior tibialis tendon behind the malleolus; the functional testing of this muscle caused pain localized in this area. Anteroposterior, lateral, and mortise x-rays "failed to reveal any abnormality." In view of the fact that this patient had had multiple injections of procaine and hydrocortisone in this area, the diagnosis of chronic tenosynovitis was made and operation for release of the tendon sheath was recommended.

At operation on Aug. 2nd this diagnosis was confirmed, and crystalline deposits were found in the area explored. An interesting laboratory finding was a high blood uric acid level. In view of this finding, he was seen by consultants to appraise the possibility of gout. He played football this past fall with continued symptoms somewhat alleviated temporarily by frequent injections of procaine hydrochloride. After the operation the patient was seen in December, 1957, and January, 1958, and in the evaluation by the arthritis unit of the University of Michigan no specific diagnosis of arthritis could be proved. Laboratory tests failed to reveal any elevation in the blood uric acid level. Diagnosis was tendinitis of the right posterior tibial tendon.

Summary

With the great increase in sports participation in schools and colleges, it behooves those interested in reducing the incidence of injury in sports to organize sufficiently accurate reports of types of injuries and the disability period of each. To determine the true incidence of injury in sports on a national or regional basis, we must record and report. Each sports participant should be conscious of his "bill of rights."

Coaches of high school and college teams should be relieved of responsibility for all athletic injury, and a team physician should be present at all contact sports sessions, whether practice or game. He, and he alone, must assume all medical prerogatives.

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PROTECTING THE BOXER

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Boxing is truly an international sport whose members represent many creeds, races, religions, and nationalities. Its popularity and wide appeal in this country have made it the great American pastime of contemporary sports. It is classified as one of the so-called body-contact sports, along with baseball, football, basketball, hockey, and other similar games, during the performance of which actual body-contact occurs. In boxing, this contact is not only more frequent but often more severe and, on occasion, serious injuries or, rarely, a fatality may result. Thus, boxing has often been considered the most dangerous of all the competitive sports.

Until recently, little thought or concern was given to the safety and welfare of the boxer, in or out of the ring. Many factors contributed to this apathy and apparent negligence, the most important of which was that the very nature and concept of the sport were such that any added measures, other

It is possible to prevent death and severe disability in boxers by enforcing certain medical standards and requirements. These include an adequate medical department, basic medical examination of boxers, adequate supervision and equipment at the ringside, periodic examination and retirement of boxers handicapped by previous injuries, semiannual physical examination of referees, and annual examination of judges. Boxers in New York state must be licensed on the basis of rigid annual examinations, and two physicians are required to be at the ringside for all bouts in that state. Systematic research into types and causes of injury, especially to the brain, the kidneys, and the skin, has led to substantial gains in safety. These gains are manifest not only in recent statistics for injuries and mortality but also in the liberalization of policies granted to boxers by insurance companies.

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than the boxers' physical endurance and ability, were not only unnecessary but harmful to the best interests of boxing. The serious injuries incurred in boxing have too often been accepted and explained as unfortunate but unavoidable accidents, inherent in the sport.

The time-honored skills in which the art of self-defense and offense are basic remain the most reliable weapons in the protection of the boxer in the ring. There is no genuine substitute for these defensive skills and offensive tactics, and they can be attained only by a carefully planned and supervised boxing program. Relatively few boxers, endowed with natural ability and athletic talent supported by adequate training and experience, have been so fortunate as to escape serious injury during their ring careers without the aid of additional safety precautions and medical supervision.

The amateur is generally more closely supervised and carefully protected than the professional boxer. The protection which is so necessary to the amateur boxer in this developmental stage of his ring career is in direct proportion to the intimate relationship with and the personal interest given him by his local club or the social or religious organization through which he is sponsored.

The professional boxer is not so fortunate, and for years professional boxing has universally been considered the most dangerous and risky of all the competitive sports. There will always remain a small but persistent minority who sincerely believe that the dangers and disadvantages inherent in boxing far outweigh any positive values claimed for the sport and that it should be abolished. Many sports authorities and physicians mistakenly believe that the incidence of fatalities and serious injuries is greater in boxing than in any of the other body-contact sports.

Gonzales,[1] in a report of fatalities in competitive sports based on a study over a 32-year period from 1918 to 1950, found that there were more deaths in both baseball and football than in boxing during that period: 43 in baseball, 22 in football, and 21 in boxing. His conclusions based on that study were that "32 years of boxing competitions have produced fewer deaths than occur in baseball or football, in proportion to the number of participants, and far fewer deaths than result from daily accidents. It seems that the moral and physical benefits derived from boxing far outweigh the dangers inherent in it or any of the other competitive sports."

The nature, methods, and objectives that have traditionally been identified with professional boxing have been considered so absolute and all-important that any medical supervision or measures for the protection of the boxer have often been reluctantly accepted by him or rejected by those promoters in charge of boxing. The old concept of winning at any price or "going down like a champ" has all too frequently exposed the boxer to unnecessary risks and serious injuries. An equally untenable and inhuman practice of permitting the fight to continue just for the sake of pleasing a few irate and frenzied fans at ringside, even though it is apparent to any impartial observer that a catastrophe is imminent, has produced mounting criticism and disfavor of the sport.

From 1946 to 1951, seven deaths occurred among professional boxers in New York state. This was a marked increase over former years and it clearly revealed the need for better medical supervision and more adequate safety precautions in professional boxing. Unfortunately, there has been little interest shown by physicians and sports officials, or by the medical profession generally, in the medical aspects of professional sports.[2] This applies particularly to boxing, in which there are no available statistics or data sufficiently accurate or informative enough to be of value in determining the medical status of boxing, past or present. Furthermore, there are factors inherent in boxing which have made it difficult to plan or establish any long-range or satisfactory medical program for this sport. Unlike baseball, football, and basketball, which are seasonal team sports, boxing is an individual, year-round sport and the average boxer is a globe trotter and does not confine his ring activities to any one state or locality.

New York State Athletic Commission

In New York state, professional boxing, since 1920, has been under the supervision and control of the State Athletic Commission, appointed by the governor. The chairmen and other members have consistently been men of outstanding ability and accomplishments in government, business, law, and sports. Their contributions to boxing have been many and varied, and the great strides and advancements which have been made in this sport over the past 35 years have been made possible largely because of the commission's humane interest in and deep concern for the personal safety and welfare of the boxer.

Up until 1948, the local clubs and the boxers' managers assumed the financial responsibility for the medical welfare of their boxers. The commission approved physicians who examined the boxers and acted as ringside doctors and were experienced and capable men, many of whom have spent most of their professional careers in boxing. Dr. Vincent Nardiello was the dean of boxing and ringside physicians until his voluntary retirement in 1957. He has unquestionably examined more boxers and served as ringside physician at more bouts than any doctor in ring history, and he has properly become the family doctor and medical adviser to a number of boxers and sports officials identified with boxing. It is largely due to the untiring efforts and services rendered by such dedicated physicians that many boxers have been spared from serious injury and disability during their ring careers. Moreover, their contributions to the medical phase of boxing has made possible much of the progress which has been made in professional boxing today.

As in other sports and occupations, the performance of which may be hazardous and dangerous at times, a decision had to be made concerning the future of boxing in New York state. Skepticism and doubts by many sports-minded individuals and groups and ardent boxing fans were expressed. Further opposition by those who have traditionally opposed boxing in any form, insisting that it could never be made a safe and humane sport, served only to confuse and prejudice the thinking of fair-minded and impartial officials. Against this confusing background was the usual problem of the cost and financial responsibility of any worthwhile medical program for boxers. The boxer could not afford to and the clubs and promoters could not be depended upon to finance and maintain such a program.

Fortunately for boxing, the state expressed its complete confidence in the sport and faith in the boxer, as it had on previous occasions when the future was threatened. It accepted its responsibility for and discharged its obligations to the boxer by the appropriation of the necessary funds for the establishment and maintenance of the first comprehensive long-range program for boxing. A brief outline and discussion of the organization and functions of the medical department and its accomplishments over the past six years, during which time most of its measures and recommendations were in operation, form the basis of this report. Included is a statistical study of the medical results achieved in boxing during this six-year period, from 1952 to 1957.

The first medical advisory board for boxing was formed in New York when Governor Dewey appointed this body in 1948. It consisted of nine members, including a chairman all of whom are outstanding specialists from medical schools and leading hospitals in the state. These authorities in sports medicine included a neurologist, psychiatrist, orthopedist, ophthalmologist, internist, physician in industrial medicine, surgeon, and dentist. While, theoretically, this board was primarily created to serve in an advisory capacity, the athletic commission wisely recognized and respected the scientific and medical achievements of this board to the extent that it was given the responsibility and authority in establishing and maintaining a comprehensive medical program for boxing.

Under the leadership of the present chairman, Dr. Marvin A. Stevens, an orthopedic surgeon who for years was a prominent football coach and is a recognized authority in sports medicine, nearly all of the many medical recommendations and safety measures sponsored by the medical advisory board have been approved and adopted by the commission. Most of this program has previously been reported in outline form.[3] Hence, only those measures which have been either omitted or only briefly mentioned and have real merit will be stressed.

Medical Standards for Boxing

Medical standards and requirements for boxing are (1) a modern, adequately staffed and equipped medical department, (2) basic standards and requirements for the medical examination of boxers, (3) adequate medical supervision and equipment for the boxer at ringside, (4) periodic examination and evaluation of poor medical and boxing risks, and, (5) semiannual physical examination of referees and annual examination of judges. There are now 36 commission-approved physicians for the examination of boxers in New York state. There are two full-time, trained technicians who take x-rays, electrocardiograms, and electroencephalograms and do the routine laboratory work required on boxers and officials. The medical department is completely equipped with all the facilities and instruments necessary for the physical examination of the boxer.

Each boxer before being licensed to box in New York state must receive and pass a rigid annual physical examination, including routine x-ray of heart and lungs, electroencephalogram, blood and urine examination, and other special examinations as indicated. Special attention is given to examination of the eyes, and there is a minimum requirement of 20/100 vision in either eye (which can be corrected to normal with glasses) with no demonstrable pathology in either eye. Additional routine examinations include the five-day prebout physical, noon-day weigh-in, and immediate prebout and postbout examinations. These findings are recorded on appropriate record and injury report forms. Special attention is given those boxers who sustain a knockout and they are required to have a neurological examination and an electroencephalogram before reinstatement.

Since 1952, two physicians are required to be at ringside for all bouts in New York state. They are supplied with a well-equipped medical kit containing first-aid dressings, suture materials, antiseptics, and appropriate drugs for the resuscitation and emergency treatment of the injured boxer.

All boxers who are susceptible to recurrent injuries or who sustain six or more consecutive losses are carefully evaluated by the commission and reexamined by the medical department. Such individuals are considered candidates for serious injury, and accordingly most of them have been medically disapproved by the board and retired by the commission. It is felt that this precautionary measure has saved many boxers from serious injury or possibly a fatality in the ring. Another valuable safety measure to spare the boxer further and possibly more serious injury is the timely intervention by the referee in stopping the fight on either his decision or that of the ringside physician. Even today far too many fights are allowed to continue when the boxer is helpless, with his arms dangling at his side and taking an unmerciful beating by his opponent. Such an uneven and one-sided contest should be halted minutes earlier rather than seconds later.

Safety measures and equipment required at ringside include (1) a new type ring padding replacing the old felt pad, (2) substitution of 8-oz. for 6-oz. gloves for all except championship bouts, (3) properly fitted mouthpieces to be worn by the boxer during the fight, (4) a portable resuscitator with oxygen equipment, available at all rings, and (5) 30-day automatic minimum suspension for any boxer who sustains a knockout, technical knockout, or other injuries of sufficient severity.

The replacement of the old felt padding by the new plastic ensolite fiber board pad (the result of over two years of exhaustive research), under the ring canvas, has largely eliminated the fatalities from serious head injuries, which were so prevalent when the old felt pad was in use. There is no longer in evidence the back and forth rocking of the head on impact of the occiput against the ring canvas which was commonly observed before this new type of pad was introduced. It is generally believed that this so-called acceleration-deceleration phenomenon which resulted from a knockout, as previously described, was the cause of those direct and contrecoup injuries and serious hemorrhages in the brains of boxers. Certainly, the incidence and severity of head injuries in boxers have been significantly fewer since this safety device was introduced.

The automatic 30-day minimum rest period, which is also honored by all states and municipalities who have a reciprocal working agreement with the New York Athletic Commission, prevents the injured boxer from getting back into the ring before he has been pronounced physically fit for fighting. The various commissions are simultaneously notified by bulletin when the boxer has been medically approved to resume fighting.

Clinical Investigation of Trauma

Clinical investigation and studies of various types of trauma associated with boxing include (1) ringside study of knockouts and frequency of head blows correlated with neurological examination and electroencephalographic patterns, (2) examinations before and after bouts to determine urologic trauma, and (3) comparison of the abrasive and irritant effects of rosin versus calcium carbonate.

The study of "Observations on the Clinical and Brain Wave Patterns of Professional Boxers," by Kaplan and Browder,[4] was reported in 1954 before the section on nervous and mental diseases of the American Medical Association. This marked the first attempt of any experienced neurologist to observe and study at first hand during the progress of a fight, and immediately thereafter, the average number of blows to the chin and head of boxers in the course of a fight and the pathophysiological changes which contribute to and result from a knockout. Kaplan served in the capacity of ringside physician while conducting these investigations, and in addition to his detailed observations made movies including slow-motion pictures of many encounters, with special emphasis on head blows, in particular those producing knockouts. He noted that most of the blows aimed at the chin or head were either blocked or fell far short of their mark.

His observations and deductions concerning the most probable causes of a knockout and unconsciousness from a blow to the chin or head are as follows: "A blow from a human being with a padded gloved fist probably is not forceful enough to produce any direct damage to the brain. Most dazed and unconscious states are due to an excessive inflow of stimuli from many sources. I actually believe that boxers become unconscious from a head blow because of the very rapid turning of the head when it is struck, thereby activating the vestibular mechanism to excess. Similarly, a blow to the abdomen may produce stimuli to the nerves in that area and cause an excessive inflow of impulses to the reticular area of the brain stem. When the cells in the reticular mechanism receive this tremendous bombardment of incoming nerve impulses, they may block off for a period of time. Any severe pain can cause a person to become unconscious in a similar manner. This may be a protective mechanism on the part of the body. I realize that this is highly theoretical, but it is certainly as good as any of the present day theories."[5] Certainly, Kaplan's observations and deductions are based on an abundance of clinical and laboratory data, as there are now available over 3,000 serial electroencephalograms in boxers. He has challenged the so-called punch drunk syndrome, originally described by Martland[6] in professional boxers, and more recently revived and emphasized by Jokl.[7] Kaplan believes that the clinical picture and pathological findings associated with this syndrome are not peculiar to boxers but have been found in the average populace as frequently as in professional boxers.

There have been two excellent studies of urologic trauma in boxers; one is a report on acute renal trauma in boxers by Amelar and Solomon.[8] They reported on the prebout and postbout urine examinations in 103 professional boxers: albumin appeared in 68%; red blood cells in 73%; and granular or hyaline casts in 26%. They concluded that the effects of acute renal trauma sustained during a fight can be determined in part by an appropriate urinalysis and that further investigations were indicated on a broader basis to determine the true incidence, severity, and effects of urologic trauma in boxers.

The other and more complete investigation of urologic trauma in boxers was conducted by Kleiman,[9] a urologist. He analyzed the results of his studies of 764 boxers over a three-year period and stated that there should be a thorough clinical and laboratory investigation of any candidate for boxing who has a history of any genitourinary disorder or renal pathology. Excretory urography should be included, when indicated. Kleiman conclusively demonstrated that trauma to the kidney by boxing, when superimposed upon preexisting pathology or anomaly, may justify the retirement of the boxer because of the likelihood of serious renal damage. In contrast, in a study of 20 retired boxers, a complete urologic survey did not reveal any pathology that would not ordinarily have been present in any similar group of nonboxers.

Dr. Max Moses[10] performed experiments in determining the relative superiority of calcium carbonate (talc) versus rosin as antislip agent and as to their respective irritating properties in the eye and on open wounds. Adult albino rabbits were used. His conclusions were that while calcium carbonate was slightly less irritating to the eye and in wounds, it produced a foreign body reaction and was more difficult to remove. Rosin was far superior as an antislip agent, and over-all rosin is superior to calcium carbonate and should not be replaced by it on the ring canvas.

Medical evaluation and statistical report of a six-year study, 1952-1957, of professional boxing in New York state revealed that of 9,871 participating boxers there were 259 knockouts, 718 technical knockouts (502 as a result of injury and 216 from inability to defend self), 9 serious head injuries requiring hospitalization, 16 eye injuries (11 corneal injuries and 5 detached retina), 29 fractures (12 metacarpal, 11 nasal, 3 of the jaw [mandible], and 3 of the phalanges), and 4 dislocations of the shoulder; 138 boxers retired or were denied license, and there were no deaths.

The absence of mortality or serious injuries in boxers during this period (there were seven deaths in the six-year period just preceding this study) is gratifying and indicates that these favorable results justify the belief and confidence in a medical program as outlined which has proved adequate for the maximum safety and welfare of the boxer. This confidence has been further demonstrated by the sizable increase of medical benefits from $500 to $750 and death benefits from $3,500 to $7,000, and these were effected without any increase of premium rates to the boxer.

Summary

The New York State Athletic Commission and its medical advisors have advocated and adopted medical measures and recommendations for the safety and welfare of the boxer. These many and varied medical measures, safety precautions, standards, and requirements, including clinical studies and research, can make boxing safer. The absence of mortality and the relatively few serious injuries in this group (less than that observed in other body-contact sports), as revealed by the medical statistics involving 9,871 boxers who actively participated in boxing during the six-year period, 1952 to 1957, when this program was enforced, strengthens confidence in the efficacy of this program in the protection of the boxer. Professional boxing can survive and prosper under such a program.

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The Cornell Aeronautical Laboratories of Buffalo, N. Y., produced the plastic ensolite fiber board pad. The Lederle Laboratories, Division of American Cyanamid Co. of Pearl River, N. Y., made the experiments on rosin versus calcium carbonate for the ring canvas.

Miss Alice Oliveri and Miss Kathy Holadak performed the laboratory and technical work for this study.

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PENETRATING RADIATION FOR CANCER.—Since there has been no significant increase in cancer cure rates in recent years that can be attributed to the treatment method alone, new and more radical procedures have been introduced in an effort to improve the results. In radiation therapy this has taken the form of supervoltage generators and the use of high energy sources of radiation such as Cobalt 60 and Cesium 137. As this trend gains momentum, the place and future of orthovoltage therapeutic radiation (250 to 400 kilovolts) must be considered. General agreement is that supervoltage radiation offers an increase in depth dose and fewer local and systemic reactions, but it is too early to assess any change in cure rate. Measured against this is the danger of deep tissue damage, less relative biological efficiency and increased costs. In view of our ignorance regarding cancer, abandoning proved procedures prematurely is unjustified. The most promising trend lies in improved training and in the skillful use of what we have.—S. R. Baker, M.D., Orthovoltage Therapy, *California Medicine,* December, 1958.

PREVENTION AND TREATMENT OF SKI INJURIES

Hans Kraus, M.D., New York

Injuries are less frequent in skiers who are in good physical condition, are skilled, and have good equipment. The treatment of most injuries in skiing mishaps is based on general orthopedic principles, but the idea of immediate mobilization needs to be emphasized. If pain and muscle spasm make mobilization difficult, the necessary exercise can generally be given after use of an ethyl chloride spray on the painful area, provided major ligament tears are excluded. There is no adequate explanation for the deep effect of the surface anesthesia, but the pain-free interval can be used to restore the muscle to normal function. Four case histories illustrate the complete rehabilitation of patients with fractures of the humerus, pelvis, and ankle and partial tear of the medial collateral ligament of the knee.

Skiing is here to stay. Its ever-increasing popularity can be witnessed by the number of ski resorts and lodges that have sprung up in all parts of the United States, by the special trains and other transportation facilities provided when "conditions" are right, by the publications devoted to this subject, by the endless conversations of the ski enthusiasts, and by the fact that, even if Nature doesn't provide snow on the slopes, man will make it!

Yes, skiing is here to stay—but with it comes the problem which is the subject of this paper, namely, the "ski injury." There are two main causes of injury: lack of skill and lack of proper physical condition. The prevention and the treatment of ski injuries create a definite and interesting problem to any physician in the United States today.

The value of the lessons learned in the treatment of ski injuries exceeds the particular application. It can be used to great advantage in the management of other athletic injuries, as well as occupational injuries.

In an effort to supplement available literature and our own experience, questionnaires were sent out to a number of physicians in skiing resorts, to ski patrol men, to ski schools, and to prominent skiers. The answers received [1] added substantially to our information on the cause and prevention of ski injuries.

Athletic injuries are those produced by circumstances inherent in respective athletic performances. They are, therefore, characterized by exposure to recurrent identical trauma and strain, making reinjury likely. Treatment includes managing the injury itself, avoiding recurrence, and permitting return to the activity as soon as possible.

Ski injuries in particular show very typical recurring hazards, which can be dealt with and which can be minimized. Since skiers usually insist on returning to their sport as quickly as possible and since this invariably offers an opportunity for identical trauma, an interesting treatment problem is presented, primarily in the phase of rehabilitation; that is, restoration of function to the greatest possible degree in the shortest possible time.

Just as rehabilitation of the ski injury deals primarily with restoration of muscle function (i. e., normal strength and flexibility in injured part), prevention of ski injury deals with assuring the skier of minimum physical requirements for safe conduct of the sport.

It is difficult to prove to what degree the physical condition of a skier is responsible for accidents. Figures available have to be evaluated with care. However, some definite information points to the fact that good physical condition is extremely important. Two instances may serve as illustrations: 1. A Westchester, N. Y., ski club averaged 5,000 skiing days during 11 years. During this time pre-ski conditioning was practiced. No fractures, and only two mild sprains, occurred. When the pre-ski conditioning was given up, three fractures occurred during the first year. 2. At the North Country School, Lake Placid, N. Y., similar facts are shown. An enrollment of 50 children, aged 8 to 14 years, accumulated a total of 5,000 skiing hours. Seven fractures and five sprains occurred. When a pre-ski conditioning program was adopted, none of the children participating in the program suffered accidents in the first year (5,000 skiing hours); two boys who did not do conditioning work suffered fractures of the leg.

The fact that ski injuries occur rarely in ski schools is well established. At the Mt. Mansfield Ski School only one fracture occurred in 7,310 hours of instruction, and in Switzerland there was only one "accident" in 3,498 hours of instruction.

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Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Prevention

The most important factor in preventing ski injuries is the skier himself. Most ski injuries are due to insufficient know-how or to poor physical condition of the skier. Speed, snow conditions, visibility, and trail conditions are hazards only when they are not properly recognized and managed.

The statistical evaluation of ski injuries is more difficult to ascertain than that of any other athletic injury. In order to compare figures accurately, they would have to be computed in terms of downhill feet, and though this has been done in some instances even this computation compares unequals; 1,000 ft. of downhill run by an expert cannot be compared to the amount of skiing done by a beginner or a racer.

It is obvious, even to the uninitiated, that equipment plays an important role in the prevention of ski injuries. A survey, supported by most personal opinions, reveals that, while release bindings are by no means safety bindings, they do offer a worthwhile improvement on the chance of avoiding injury. At Garmisch-Partenkirchen, Germany, of 17,500 persons who rented nonrelease bindings, 74 sustained fractures; of 45,043 who rented release bindings, 11 sustained fractures. At Stowe, Vt., nonrelease bindings were used by 48% of skiers, in which group 66% of accidents occurred.[2] Also, the use of less pointed poles would decrease some of the stab injuries. Sharp edges have increased the incidence of cuts, but it is unlikely that this, even if generally known, would persuade any skier to make a change.[1c] Clothing and boots have now been generally developed to the point where most skiers are properly protected. And, since skiing areas are usually close enough to warming facilities, frostbite is not a serious hazard.

As mentioned, strength and flexibility of the skier play the largest part in avoiding injuries by making fatigue less likely and by improving the ability of the skier to meet inevitable spills.[1] A physically adequate skier will know when he is warmed up and will consciously try for warm-up by some uphill walking and cross-country running, and this same skier will realize when he is tired and will avoid that famous last run.

Treatment

Formerly the injured skier came in with the question, "Can I ski again?" Now, even the more severely injured come in with the question, "When can I ski again?"

The management of ski injuries, which, of course, basically rests on generally accepted orthopedic principles, is thereby given an added problem, namely, how to restore full function in the shortest possible time. Attempts to answer this demand have resulted in experience valuable in the treatment of other athletic injuries as well as occupational injuries. The special problem of ski injuries is one of rehabilitation and, more specifically, one of restoration of muscle strength and flexibility.

Clay Ray Murray and William Darrach used to say that the ideal treatment of fractures would be to "wish the bone back in place, to keep them there by a wish, and to start active motion of the injured parts at once." It is this principle that made them advocate open reduction and internal fixation wherever possible. The best treatment is immediate mobilization, not only where internal or external fixation have been necessary but also where immobilization can be eliminated by immediate active measures.

A contraindication to immediate movement is pain and subsequent muscle spasm. Use of local measures in treating the pain and spasm make it feasible to immediately mobilize not only sprains and strains but fractures as well if the position is acceptable and displacement does not have to be feared.

Fractures treated by immediate mobilization include fractures of the pelvis (os pubis), fractures without displacement of the short bones of the foot (intraboot injury),[1a] fractures of the head of the humerus, fractures of the metacarpals, fractures of vertebrae, if uncomplicated and if no pedicles are involved,[3] fracture of transverse processes of vertebrae, and fractures of the ankle without displacement of the lateral malleolus, if not combined with ligament tear. We prefer immediate mobilization for reduced dislocations of the shoulder and elbow, and for fractures of the tuberosity of the humerus. At New York University–Bellevue Medical Center fractures treated over a period of about two years included impacted humerus (87), pelvis (62), vertebrae (47), metatarsal (63), calcaneus (43), and tibial plateau (38).

Immediate mobilization of sprains of the ankle and knee and strains of the lower part of the back, of the calf, or of the hamstring tendons restores function[4] in a shorter period of time, and if followed by adequate therapeutic exercises produces better long-range results. Of 126 persons with injury of the medial collateral ligament of the knee, 51 (40%) had had previous injury. Of 70 who were followed for from 2 to 15 years, none had reinjuries, 62 had skied again, with no complaint, 5 had not skied again, and 3 had skied again, with reactions of pain and swelling.

Before deciding on immediate mobilization, however, it is important to exclude major ligament tears, especially in ankle injuries (fig. 1). Tears in the collateral ligament or intraosseal ligament as well as tears of the medial collateral ligament or cruciate ligament of the knee are not to be classified as sprains. They frequently need surgical repair, sometimes immobilization in plaster casts. The following case histories may serve as illustrations.

Report of Cases

Case 1.—The patient fell while skiing on March 3, 1956. X-rays showed comminuted fracture of the anatomical and surgical neck and greater tuberosity of the right humerus. He was seen in consultation by Dr. Frank Stinchfield. At his suggestion immediate mobilization was started. The patient came to see me on March 9 for the first treatment, which consisted of surface anesthesia and exercises. On March 23 there was no pain and abduction was possible to 90 degrees and scapula-humerus abduction to 80 degrees. There was steady improvement. On May 18, 1956, there was some limitation of inward rotation but otherwise full range with slight residual weakness. The patient had been skiing since three weeks after the accident without discomfort. On reexamination Nov. 30, 1956, he had full range and power, with no complaints. At follow-up examination there were no complaints (fig. 2).

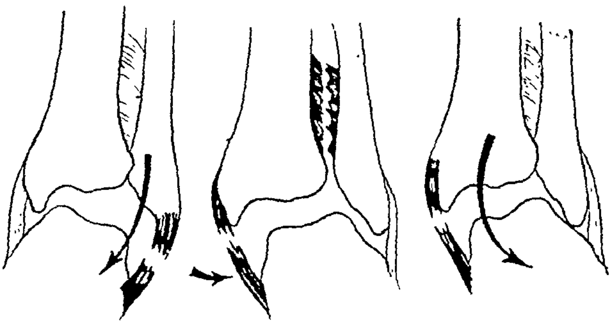

Fig. 1.—Serious injuries, drawn from x-ray negative. *Left,* lateral collateral ligament; *middle,* inferior tibiofibular ligament; *right,* medial collateral ligament. (Supplied by Charles Neer.)

Case 2.—The patient fell while skiing on Dec. 29, 1948. This patient was placed in a hammock at a local hospital. X-rays showed evidence of fracture of the pelvis with fracture site located in the inferior ramus of the pubis and at the junction of the superior ramus of the pubis with the ischium, both on the left side. Traction was suggested. The patient could not void and was extremely uncomfortable. I saw the patient on Dec. 30, 1948. Therapy was started immediately with ethyl chloride spray and exercises. Immediately after removal from the hammock and start of active motion exercises and ethyl chloride spray, the patient improved and voided spontaneously. On Jan. 3, 1949, partial weight-bearing was permitted and gradually increased. Two weeks after the accident the patient returned to college. On reexamination Jan. 31, 1949, there was no atrophy and the patient had no complaints. At follow-up examination there were no complaints. The patient is able to ski.

Case 3.—The patient fell while skiing on Feb. 26, 1953, and suffered a fractured ankle. Stress pictures showed some medial displacement. The patient was a ski instructor, therefore surgery was recommended (Dr. Frank Stinchfield). There was a complete tear of the deltoid ligament which was repaired, and a Rush nail was inserted to the lateral malleolus. The patient's ankle was in a plaster cast until March 10th, then was placed in half-shell cast. The exercise regimen was supported by electrotherapy. On March 31, 1953, the patient had full range of motion with exception of some limitation of *Vorlage* and inversion. Treatment was continued until April 1st when the patient left New York with his leg in a short leg brace. There was almost full range of motion in the ankle joint and good strength. At follow-up examin in February, 1958, the patient stated he had been skiing e since with no difficulties (fig. 3).

Case 4.—The patient was first seen on Jan. 25, 1939. He had fallen while skiing and twisted his right knee eight d prior to visit. The history revealed a football injury 10 ye previously with repeated episodes of knee injury with swelling. The present diagnosis was partial tear of medial collater ligament, considerable effusion, and marked vastus atroph. The patient came in daily for ethyl chloride spray and exercises and was free of pain by Feb. 2, 1939. He skied again, against advice, on March 2nd and returned from skiing with some pain and swelling. Treatment was resumed. Operati was considered but the patient wished to continue on conservative regimen. He improved on therapy with exercis and ethyl chloride spray and was almost fully rehabilitated by May 27th. This patient has been followed closely, as h has returned with various other ski injuries. However, he ha had no further difficulty with the treated knee.

Comment.—This patient had had a number of injuries t the knee joint. These episodes ceased entirely after rehabili tation to complete strength.

Technique of Immediate Mobilization

The technique of immediate mobilization in cludes local relief of pain and therapeutic exercise as the most important factor in the treatment o athletic injuries.[5] A brief description of the tech nique follows.

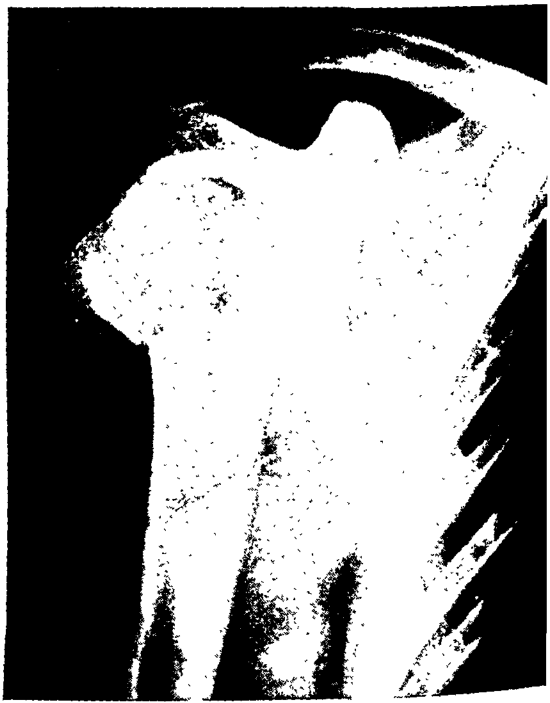

Fig. 2 (case 1).—Comminuted fracture of anatomi and surgical neck and greater tuberosity of right humer

The pain is located by active motion. Eth chloride is then sprayed on this area. The patie then starts active movement of the part involve in the direction in which motion has been painf and limited. As the patient increases his range, ne painful areas will develop. These areas must aga be sprayed, and active motion continued. Treatments last from 10 to 30 minutes, and should be carried out within limits of pain.

Immediate use of the affected part may be allowed in patients able to perform normal movement, but excessive strain and sudden movement should be prohibited. Patients with more severe disabilities should be advised to rest, but all patients should be urged to continue the active movements that they have been taught. The exercises should be performed from a minimum of twice a day to as often as once every hour, for approximately five minutes. While a single treatment will suffice in cases of minor involvement, patients with more serious difficulty require frequent treatment: daily during the first week and later every other day (fig. 4).

An effective treatment should not require the application of anesthetic after the second week. Therapeutic exercises must continue, and increase in scope, until normal muscle power is restored. Once motion is instituted, immobilization should not be used, as it is contrary to the basic principle. It should be stressed that active motion, though unquestionably necessary, should never be brusque or abrupt so that painful spasm in muscles will not be further aggravated.

Compared with injection of procaine hydrochloride into the muscles and ligaments, the use of ethyl chloride has certain definite advantages: 1. The application is simple. 2. Repeated application is possible with minimum difficulty and risk. 3. Large areas can be controlled that would otherwise require quantities of procaine hydrochloride. 4. Ethyl chloride does not mask bone or ligament injury. 5. It is better as a diagnostic means, since it is more selective. 6. There is less risk of a local after-effect and there is no general after-effect, such as occasionally occurs after the administration of procaine hydrochloride. 7. There is no danger of infection.

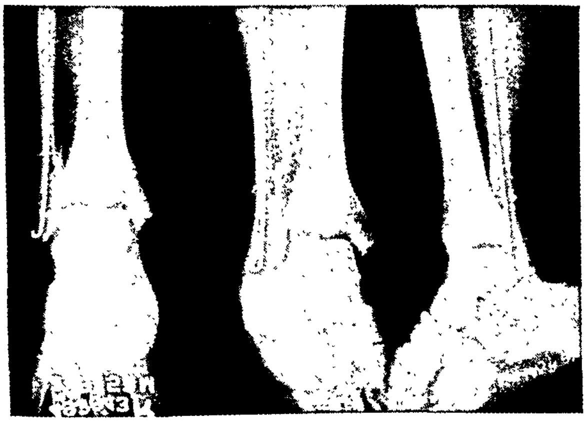

Fig. 3 (case 3).—Fracture of distal end of fibula, with fixation.

The administration of surface anesthesia is only the first step in the treatment of painful muscle spasm. Exercise is the necessary second step. Without it, the use of surface anesthesia would accomplish little more than the use of gas or ether in surgery without operation.

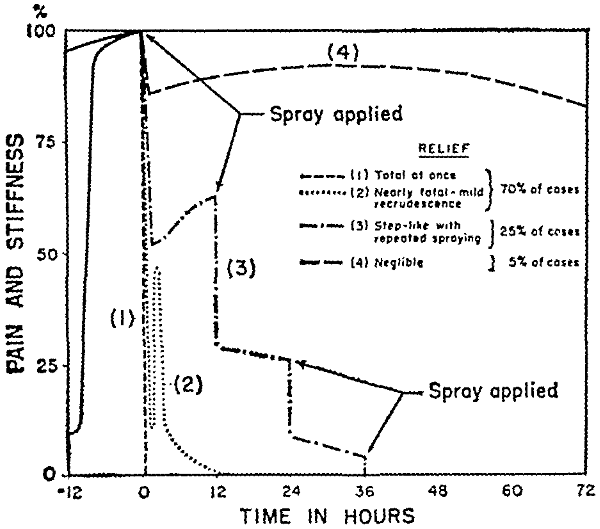

Fig. 4.—Response of acute "stiff neck" to ethyl chloride spray. (Reproduced from Travell,[4d] with permission of *Archives of Physical Medicine and Rehabilitation.*)

Exercises must be performed immediately after application of the anesthesia. These should be exercises to restore elasticity and increase relaxation and length of muscle and should always be performed below pain and fatigue limits. Scattered dosage from two to five minutes, and exercises every one-half to one hour should follow. The supporting prescription may call for particular or complete rest between exercises.

The most common mistakes made in treatment with surface anesthetics and exercises are (*a*) failure to cover the full painful area with anesthetic, (*b*) overdosage of violent exercise, (*c*) neglect of pain limit, (*d*) neglect of home exercises, (*e*) neglect of supportive prescriptions, (*f*) neglect of follow-up treatments, (*g*) failure to explain properly to the patient and to arouse the necessary cooperation, and (*h*) faulty indication.

As to the theory involved: Pain originating in one portion of the sensory motor chain leads to reflex muscular spasm and locking of joints (fig. 5). This sensory motor chain consists of the following elements: Sensory nerve, nerve center, motor nerve, muscle and sensory nerve. Pain originating in the course of this chain leads to muscular spasm. Elimination of pain at any point in the chain results in the breaking of the chain, and, therefore, in relaxation of the muscular spasm. This may be achieved directly by the injection of an anesthetic into the muscle, joint ligament, sensory nerve, or spinal cord.

If the pain-free interval is used to restore the muscle to normal function, spasm does not recur, or it recurs with much less intensity. It has been our experience that, on the basis of this chain, cutaneous anesthesia similarly relieves deep-seated pain in muscular spasm.

There is no adequate scientific explanation for the deep effect of surface anesthesia. However, the underlying physiological reason presents an interesting field for exploration. And, it should again be emphasized that surface anesthesia alone, without active motion, will not achieve good results.

When the acute phase has subsided, strengthening exercises to weak muscles, as well as limbering and stretching exercises to tight muscles, must gradually be increased. To be of value these exercises must exceed easy performance and at the same time should cease before the point of fatigue so as to avoid setbacks.[4a]

As soon as the joint can be moved through full range, weight lifting exercises may be added to resistive exercises; but weight exercises are not a substitute for resistive exercises. The weight tolerated through full range is by necessity smaller than the maximum range tolerated in a particular section of the movement.[4a] Active resistance adjusting to these different potentials can, therefore, give a more efficient and complete workout. As long as there is little exercise tolerance, daily sessions are necessary and should be supplemented by frequent periods of movement at home.

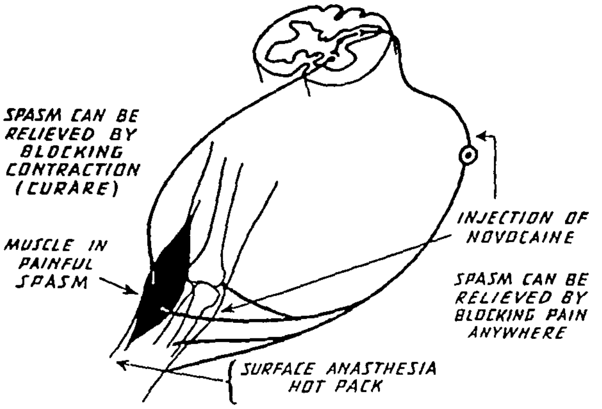
SPASM CAN BE RELIEVED BY BLOCKING CONTRACTION (CURARE)
MUSCLE IN PAINFUL SPASM
INJECTION OF NOVOCAINE
SPASM CAN BE RELIEVED BY BLOCKING PAIN ANYWHERE
SURFACE ANASTHESIA HOT PACK

Fig. 5.—Diagram showing sensory motor chain leading to reflex muscle spasm and locking of joints and method for relief.

Once strong workouts are started, three sessions per week are usually all that are necessary but should be supplemented by homework of one or two tolerance sessions each day. Of course, it is true that such extensive rehabilitation programs should be given only where return to the sport is desired, as one must remember that a knee that is perfect for city life may be in great jeopardy when exposed to the hazards of skiing.

Since it is the lower extremity that is most frequently jeopardized in skiing (see table), evaluation of the injury should include comparison of strength with contralateral side (by weight lift or scale test)[4a] (fig. 6). Full range of knee and ankle joint should be restored. The ankle joint should be especially tested on forward bend with the heel on the ground (*Vorlage*). If this movement is limited, it may well be a cause for reinjury. For example, when a skier goes over a bump and tries to bring his weight forward, he will experience a pull on the shortened muscle. This will cause him to unweight his ski, the tip will tend to dive, and the skier will fall with probable injury to the extremity.

*Distribution of Ski Injuries**

Location	%	Type	%
Head	4.3	Shock	1.1
Shoulder	1.9	Stabs	1.3
Arm-hand	2.7	Dislocation	1.5
Back-trunk	0.8	Fracture	31.5
Leg	92.0	Laceration	10.0
Miscellaneous	0.2	Sprain	51.3
		Bumps, etc.	1.9

*Data from the National Ski Patrol System.

The mere passage of time alone does not contribute to full rehabilitation. It can almost categorically be said that daily activities in the city do not prepare the skier for strenuous use of quadriceps and leg muscles nor do they give the required elasticity of the soleus which makes a leg safe for skiing. A study of 500 skiing injuries revealed that 14.2% were reinjuries. Of 126 knee injuries, 40% were reinjuries. A survey of 195 skiers, by the ski patrol at Stowe, Vt., revealed 132 had had no injuries, 41 one injury, 15 two injuries, and 7 more than two injuries.

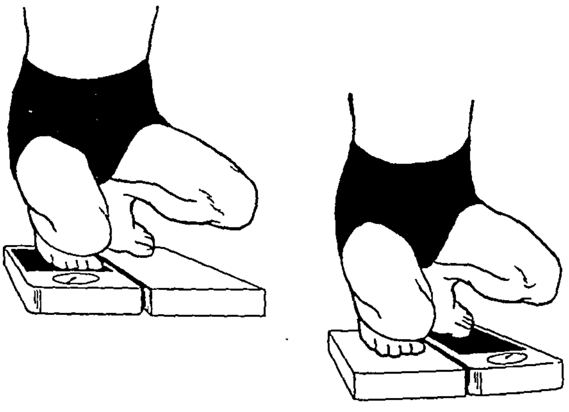

Fig. 6.—Scale test for evaluation of injury by comparison of strength with contralateral side.

Summary

Poor muscular condition is a main cause for ski injury. Physical conditioning before skiing is the best prevention. Weakness and stiffness after injury are among the main causes of reinjury. Therapeutic exercises to restore full function of the injured part are essential to make it possible for the injured skier to return to his sport safely.

The use of ethyl chloride spray and active exercises immediately after sprains, strains, and certain types of fractures has been found most effective in over 25 years of work with that method.

30 W. 59th St. (19).

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RESPIRATORY PHYSIOLOGY AND SKIN DIVING

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Skin diving with self-contained underwater breathing apparatus (scuba) has hazards that distinguish it both from free diving during short periods of voluntary apnea and from traditional diving with helmet, pump, and connecting tubes. It is also necessary to distinguish between the type of scuba in which the expired carbon dioxide is absorbed chemically, the needed oxygen is added, and the nitrogen is rebreathed from the type in which the expired air is simply discharged into the water as bubbles. Although the latter form is less dangerous, it has its hazards, including air embolism, decompression illness, nitrogen narcosis, oxygen intoxication, rupture of eardrums, and squeeze. Squeeze, the pressing of body tissues into air-filled spaces in the diving costume, is particularly damaging to the eyes. The bulging of the eyes into goggles is hard to avoid, but if a mask is worn instead of goggles the danger can be decreased by discharging air from the nose into the mask whenever pressures increase.

Skin diving as a hobby and as a sport has increased tremendously in the past 10 to 15 years. The introduction of commercially available skin diving equipment has increased the number of divers to almost a million people registered in nearly 400 clubs. Skin diving is not limited to salt water seacoast areas. There are many diving clubs even in such inland spots and inaccessible areas (as far as water goes) as the deserts of Nevada and Arizona.

An increase in accidents and fatalities is the result of the marked increase of the number of people who have taken up skin diving. In California there was approximately one death per month from January, 1953, to April, 1955, besides the many accidents which were not fatal. In skin diving the mortality in any given set of accidents is high—in contrast, for example, to skiing, where morbidity is higher compared to mortality. In order to improve the statistics of injury from skin diving, it is appropriate to describe the injuries and accidents which are associated with it and their prevention and treatment.

Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Free diving is diving after a mild or moderate amount of hyperventilation with a deep breath of air and then coming up when the breath-holding period has passed. There is no external source of compressed air or oxygen in this type of diving. In scuba diving (the letters stand for self-contained underwater breathing apparatus), a demand regulator and source of compressed air or oxygen is used and the individual breathes through a flexible rubber hose. In the case of the "compressed air" type of breathing "lungs," the compressed air is inhaled and the exhaust is released through a one-way valve into the water which bubbles to the surface. In the so-called rebreathers, there is a soda-lime chamber to absorb the carbon dioxide, only oxygen is supplied to the bag, and there is no tell-tale bubble trail on the surface.

Requirements for a safe diver include both physical and psychological components. Skin diving can be exhausting, and it is axiomatic that good physical condition is a prime requirement. Good swimming ability is of paramount importance, and familiarity with water sports in general is of tremendous value. No one with chronic cardiovascular or respiratory type of derangement should indulge in the sport. Obesity is also a detriment. Some patients should be limited to free diving in shallow water. The individual who has chronic ear trouble and who is unable to inflate the middle ear through the eustachian tubes with intranasal pressure will find that he can not dive more than 12 to 15 ft. without pain in his ears and the possibility of rupturing the drum.

There are also psychological requirements for a good or, indeed, even a safe diver. The individual who is very nervous, is easily upset, lacks self-confidence, and might panic at the onset of an emergency should never attempt to dive. The show-off type, the dare-devil who takes chances and loves to show his superiority over others, is a dangerous diver whose diving should be controlled as much as possible.

Man's general problems in skin diving are associated with the fact that he is not designed or equipped to be under water safely. The physical laws of gas behavior all impose limits on his underwater activities. Boyle's law is one of the most important. Briefly stated, Boyle's law says that if the temperature remains constant, the volume of the gas varies inversely with the pressure. The pressure at sea level is 14.7 lb. per square inch (760 mm. Hg). For each 33 ft. a diver goes below the surface, there is an increase of one full atmosphere of pressure. Therefore, at 33 ft. there are 2 atmospheres of pressure absolute; at 66 ft., 3 atmospheres; at 99 ft., 4; and so forth.

In this same context, a given volume of air in the lungs (for instance, 2,000 cc. of air) at sea level before diving will be compressed at 33 ft. below the surface to 1,000 cc. and will be compressed another 33⅓% at 66 ft., then occupying a volume of approximately 667 cc. When ascending, a diver at 33 ft. may inhale a breath of compressed air from a scuba unit, filling the lungs exactly half way, and at the surface the lungs will be completely full and the volume of gas will be twice what it was at 33 ft. Dalton's law states that each gas exerts its own tension in a mixture as though it occupied the space alone, and Henry's law states that gases dissolve according to their partial pressures in a contacting liquid. Thus, in general, the difficulty with man under water lies in the air spaces in his body. The body tissues in general are considered to be incompressible, and, in animal experiments, pressures of over 100 atmospheres have not caused noticeable damage to tissues per se.

Air Embolus

The term "air embolus" has been used to describe the accident which occurs when an individual inhales at increased pressures a full lung of air and then rises rapidly through the water to a much decreased pressure, causing a marked increase in the volume, according to Boyle's law, of the compressed air in his lungs. The lung tissue is fragile and, normally, the increased pressure behind the sternum and against the diaphragm can be felt and will usually be compensated for by a normal exhalation, but a person who is in a hurry to get to the surface is frequently in a state of panic. He may also be under the impression that he does not have enough air. A spastic glottis is the result, and the lung tissue can in a mild case be torn and in a severe case be completely ruptured with the introduction of air emboli into the pulmonary veins returning to the left side of the heart. In one case described in the literature, the air emboli were so universally distributed throughout the body that the cut surfaces of all body organs contained air and were felt to exhibit crepitations.

The signs of air embolus are, essentially, bleeding from the lung, shortness of breath, dyspnea, cyanosis, and collapse. In mild cases treatment consists of placing the patient in the head-down position and supportive therapy for shock. At times recompression to the level at which the patient was before he began to ascend in the water is of benefit. Prophylaxis, of course, in such an accident is much simpler and more effective than is treatment. If all divers understood that there is never a situation in which it would be safe to come up to a shallower depth in the water, after breathing compressed air, without a continuously open glottis and free exchange of air in and out of the lungs, such accidents would be much less common.

An interesting side-light in this particular phenomenon has to do with the individual who has, for some reason, been caught at considerable depth with either a malfunctioning scuba or, more usually, a sadly depleted air supply. If he takes a comfortably deep breath at that stage, takes his scuba mouthpiece out, and then exhales slowly at the greater depths and more and more rapidly as he gets near the surface, he will find that the air in his lungs will be discharged and he will not particularly feel the need of exhaling. This procedure is not essential, necessary, nor indicated in free diving because the diver takes in 1 atmosphere of pressurized air at the surface and dives down to 30 or 40 ft. Then on his way back up the air that was compressed at 40 ft. will expand again but can go no further in expansion than it was at the 1 atmosphere of pressure that he began with at the surface. He took in no compressed air at increased pressure below the surface of the water.

Air embolus can cause death. A diver using a scuba in 20 ft. of fresh water apparently found it suddenly difficult to breathe as the air diminished in his lung. He closed his glottis, kicked for the surface, came up and shouted to the people on shore, but sank again immediately. Postmortem examination disclosed severely shattered lungs. These divers may even die before reaching the surface.

Caisson Disease

Caisson disease (the bends) is caused by increased pressure of nitrogen when one works under pressure. The nitrogen dissolves in the blood stream at a proportion to its partial pressure, according to Henry's law. Then, on decompression from depths, the nitrogen in the tissues and in the blood stream, if not decompressed slowly enough, will cause bubbles which reabsorb slowly and cause what is called "the bends" or "the chokes." Bubbles in the blood stream and tissues cause caisson disease. At 99 ft., at an absolute pressure of 4 atmospheres, nearly 5 cc. of nitrogen is dissolved in 100 cc. of blood; thus, all of the blood of a 155-lb. (70-kg.) man would release 130 cc. of nitrogen and the tissues would release up to 10 times that much. Symptomatology of caisson disease includes pain in over 90% of all cases, associated with the area in which the bubbles are causing difficulty.

The tendons and the cerebral spinal nervous system are two of the most common places that are attacked in caisson disease. The chokes are a manifestation of nitrogen bubble emboli in the pulmonary capillary system with resultant pulmonary edema, usually quite severe. Fat people have more difficulty with caisson disease than do thin people, because of the increased nitrogen solubility in fat as compared to water. The treatment recommended in mild cases is use of recompression to 30 lb. pressure and 100% oxygen at that level for one hour. Then decompression should begin at the rate of 1 lb. of pressure per minute. In severe decompression illnesses, the treatment should be recompression to 75 lb. of pressure, with 50% oxygen, for 15 minutes to two hours, depending on symptoms, and then decompression to 30 lb. of pressure at the rate of 1 lb. per minute and maintenance on pure oxygen for one to two hours. If, however, after 1 hour with pure oxygen at the 30-lb. pressure level, the patient still has symptoms, 30-ft. breathing air is used for 24 hours, then oxygen for 2 hours, followed by 1 lb. per minute decompression rate to normal. Effective treatment in preventing caisson disease is use of a warm compression chamber if no more than three or four minutes have elapsed since the patient left the water and entered the chamber. In one experiment, in 130 dives from 66 to 108 ft. for one-half to two and one-half hours, decompression was begun in an average of six and three-tenths minutes after the divers left the water, and during these dives there were no signs of caisson disease.

For prophylaxis of caisson disease, normal U. S. Navy standard decompression tables are available to the skin diver. Briefly, the depths to which one can dive are estimated from length of time and depth in the water. For example, without any decompression it is generally safe to stay at a depth of 125 ft. for 15 minutes, 75 ft. for 35 minutes, and 30 ft. for any length of time. Time is computed from the moment of leaving the surface until leaving to come up from the greatest depth reached. It is exceptionally difficult to estimate time under water, and only a watch should be considered effective in time measurements. If a diver went 200 ft. down and stayed for 35 minutes, decompression time on coming up would be 22 minutes at 30 ft., 28 minutes at 20 ft., and 46 minutes at 10 ft., with the rise from the bottom at a rate not to exceed 25 ft. per minute, with one minute to come up from the three stops at 30, 20, and 10 ft. This gives 106 minutes of total decompression time from leaving the bottom until reaching the surface. At a depth of 300 ft. for 45 minutes, decompression time would be a total of 5¼ hours at levels from 90 to 10 ft., stopping every 10 ft. One other thing which must be kept in mind in decompression tables is that the effects of any dive which is within 12 hours of the last dive are cumulative, and the diving tables are used by computing the total time of all dives at the last depth. On trips to Catalina, for instance, frequently two or three tanks of air will be used by each diver and caisson disease is likely in a depth of usually 75 to 150 ft. because of the failure of the divers to add their diving times together.

Other Risks of Skin Diving

Nitrogen Narcosis.—The syndrome called nitrogen narcosis or "raptures of the deep" is also a result of pressure of the inhaled air. Below a level of 100 to 160 or 170 ft., depending on the individual, there is a gradually increasing feeling of exhilaration and euphoria, similar to an acute alcoholic bout and described as a feeling of wanting to remove the mouthpiece of the scuba unit and hand it to a passing fish because it is not needed. Fatal errors in judgment may occur as a result of this narcosis. There have been frequent deaths, due partly to this syndrome, of persons who have tried to break the underwater, deep-diving scuba records. The record at present is in the vicinity of 375 or 380 ft. The treatment for this syndrome is immediate return to shallower depths where symptoms immediately disappear. Prophylaxis is to stay out of the lower depths unless essential. Use of up to 90 or 95% helium with oxygen, used only at the lower depths, will relieve a marked share of the symptoms of nitrogen narcosis.

Oxygen Poisoning.—Oxygen poisoning is the name applied to a syndrome which is the result of breathing oxygen at markedly increased pressures. The depth reached before this syndrome begins varies in different persons, but generally the limit of oxygen for any length of time is considered to be about 30 ft. Some have gone down 40 or 45 ft. for one-half hour without difficulty, but the more exercise that is involved at that level the more is oxygen poisoning likely to occur. Symptoms include dizziness, headache, muscle twitching, and convulsions with coma. This syndrome occurs mainly in the rebreathing units at the shallower levels but may occur in extremely deep dives with the use of air. For instance, at a depth of 297 ft. and an absolute pressure of 10 atmospheres, the use of compressed air or even a 20% oxygen mixture with helium will give the same oxygen partial pressure as using 100% oxygen at 33 ft. Therefore, symptoms below that level can be identical with oxygen poisoning. Oxygen tensions of air which is breathed in the cylinders used in the deep diving record attempts are almost always cut down to 10 to 8% or even, for low dives, 5%, in order to minimize the possibility of oxygen poisoning. The treatment is simply to come up from the depth at which symptoms begin, and they will decrease rapidly.

Drowning.—Drowning as a result of exhaustion, oxygen lack, and carbon dioxide excess is one of the most common sources of fatalities. Exhaustion is the keynote to this type of accident, and the development of the exhaustion would be markedly increased by panic in an emergency which could cause a diver to overextend himself and ignore completely the general principles of safe diving. The symptoms are unconsciousness, cyanosis, and vasomotor collapse. The treatment is immediate and enthusiastic artificial respiration, preferably with oxygen. The prophylaxis of drowning is to remember to have available under all circumstances and at all times as many of the safety precautions and equipment as possible. One of the most effective safety measures is some type of a float with a line on it at least three times as long as the planned diving depth, with a 2-lb. or 3-lb. anchor weight on the end. This float may be an innertube or a fancy arrangement on which one can hang spear guns, fish, abalone, abalone irons, and camera and thus have an efficient piece of equipment as well as a reliable, handy place to rest. There is no way of overemphasizing the importance of having somewhere to rest when one becomes overtired or has had a harrowing experience. Many men have had nearly fatal accidents, and it behooves all divers to use their heads and take advantage of such a simple and efficient piece of apparatus as a float.

Ruptured Eardrums.—The increased pressure at depth is a mechanism which forces the eardrum to go inward toward the middle ear unless there is equalizing pressure from the middle ear to prevent it. If the eustachian tubes are closed off and air is unable to reach the middle ear from the nose, a ruptured eardrum may occur. The symptoms are acute pain in the ear and, frequently, bleeding from the external canal. Treatment is prevention of infection and prohibition of diving until healing is complete, approximately a period of eight weeks. Without infection, complications, or a severe tear, a small rupture will heal promptly and normally without difficulty. Prophylaxis depends on having the eustachian tubes as open as possible and not diving unless they are open and kept that way. Ear plugs should not be used in diving as they would, if they fit tightly, cause a rupture of the drums from the inside as soon as the pressure in the middle ear reached the pressure of the water. The free exchange of pressure into and out of the external ear is just as essential as the exchange into the middle ear through the eustachian tubes. There is an associated condition in which a rubber suit, used for warmth, can flatten out over the external canal, sealing it completely.

If the negative pressure in the external canal with the pressure bowing the drum out from the middle ear is not quite strong enough to break the drum, a blood blister may occur from the suction effect. This blister can be quite large and rupture the skin of the external canal beside the drum, with bleeding from the ear. The prophylaxis is not diving with a severe cold or when for any reason the eustachian tubes are unable to allow the transfer of air back and forth freely. An easy way to test this is to hold the nose tightly and try to blow hard through the nose so that the intranasal pressure is increased. If there are stuffy feelings in both sides through both ears, then the eustachian tubes are open and will present no difficulty. Frequently the use of propylhexedrine (Benzedrex) or some other type of an inhalant to shrink the mucous membranes will give a good exchange where swollen membranes would cause difficulty.

"Squeeze."—The phenomenon known as "squeeze" is peculiar to the use of the dry suit, which is a solid rubber sheeting arrangement encasing the body, with elastic wrist bands and a stretchable opening for the face. Means of entry is a chute in the front of the chest, and this is closed off with rubber bands. Two or three sets of wool underwear are worn inside this rubber suit for warmth. Air entrapped in this underwear by the pressure of the water may cause folding of the

skin, and the skin may actually be sucked up into little ridges and welts in the folds of the cloth because of the relative negative pressure of some of the folded areas. The ridges and welts may approximate blood blisters and last for several days. The areas with the most air entrapped are those of the poorest fit of the rubber suit, especially the genital areas, and in a male diver squeeze may be quite noticeable. Also, air from the scuba unit may be forced into the suit by snorting into the face mask, causing an increase of the amount of air inside. This is all right at 100 ft., but during ascent this same air under pressure blows up the suit like a balloon; the rate of ascent can thus get out of control, so that it may be difficult for the diver to slow to the recommended rate of 25 ft. per minute. This does not happen with a wet suit, which allows water to get inside, thereby equalizing the pressure.

The same type of a squeeze may occur as a result of a tightly fitting face mask if the individual does not realize that he needs air from inside his nose to fill in the mask. Water pressure can compress the mask sharply around the nose, face, and eyes, causing negative pressure with protrusion of the eyeballs. For this reason, in any but the mildest and most shallow of diving, diving goggles are not recommended. They allow no method of putting air inside the goggles themselves when under pressure, and, therefore, eyeball squeeze is more frequent with goggles than with masks.

Comment

These, then, are some of the difficulties which can beset a diver. Diving is a tremendous sport, exciting, interesting, and different. But the sea is a hard taskmistress and she allows comparatively little human error. With adequate preparation and precautions, diving can be safe. Without them, accidents are likely and dangerous. It behooves everyone to be as careful as possible in taking up the wonderful sport of skin diving.

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SURGICAL TREATMENT OF INJURIES TO LIGAMENTS OF THE KNEE

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The most severe forms of injuries to the knee often do not properly heal without surgical intervention. This is true whenever any major ligament is completely cut across or avulsed from its attachment, and particularly when the torn ends of one structure come to lie in positions that hinder the union of other structures. Surgical experience with over 150 cases of injury to the knee has shown that conservative treatment can be expected to lead to healing only when tears are partial. When the symptoms of pain, instability, abnormal mobility, hemarthrosis, and circumarticular effusions testify to severe injury, conservative treatment fails. The best results in such cases have been obtained when diagnosis was precise and surgical treatment prompt. Surgery is followed, on the same day, by physical therapy, which includes muscle-setting exercises (isometric contraction without joint motion) and other graded activities. A policy of complete repair and conscientious rehabilitation has given increasingly gratifying results.

While we are not primarily concerned in this discussion with the over-all treatment of injuries to the ligaments of the knee, one cannot intelligently discuss surgical treatment of such injuries unless there is some generalized discussion of the proper indications for surgery as opposed to nonsurgical measures. I have repeatedly emphasized in previous reports the necessity for an extremely accurate diagnosis of an injury to the knee if one is to be prepared to carry out the ideal treatment.[1] If one assumes that surgical treatment is never indicated for injured knee ligaments, treatment of the injured knee becomes vastly simplified. If on the other hand one is prepared to admit that there are some cases which will require surgical treatment, it becomes immediately apparent that one must be able to determine which case should be treated by surgery and which case should be treated by nonsurgical methods. If all ligament injuries are to be treated by modifications of the same basic method, it may indeed be of only academic interest to try to determine the exact pathology which is present in any given case.

Read in the Symposium on Sports and Sports Injuries in the Session on Injury in Sports before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

I think there is a general agreement that there are certain basic therapeutic measures which should be instituted in the treatment of an injured knee ligament. Individual physicians may use many variations but, in general, aspiration, local injection, compression bandage, ice pack, immobilization, local heat, protection, and finally rehabilitation are utilized to a greater or lesser degree, depending on the severity of the injury and on the inclination of the physician. If all knee injuries are to be treated alike, it may be of little importance to determine the exact pathology, since one can play it more or less by ear and regulate the number and degree of the above measures he uses according to the response of the injury to treatment. This may be the easiest and most convenient way of treating it. The fly in the ointment, of course, is that this is not the best way of treatment.

If one could safely assume that treatment may be standardized into the measures mentioned above, the problem would become quite simple. If there is effusion, aspiration may be carried out. If the effusion recurs, aspiration may be repeated. If the effusion subsides, further aspiration will not be necessary. If the injury is mild, compression may well be the only protective appliance applied, and it may soon be discarded. On the other hand, if swelling persists, compression bandages may be continued over a longer period of time and vary from the elastic bandage to the application of a cotton cast. If symptoms do not subside promptly, more adequate treatment may be carried out to the extent of applying a plaster cast, which can be worn for several months if the knee does not respond. So, if treatment is to be identical whatever the degree of the injury and whatever the ligaments involved, one could well initiate this treatment first and then decide, depending on the patient's progress, whether he was badly hurt or had a minor injury. Why then should we demand "tender but meticulously complete examination of every injury"?

Such specious reasoning, by appearing on the surface reasonable, insidiously undermines one's actual understanding of the condition which he is treating. It is easy to see how the habit of treating these injuries by "feel" rather than by diagnosis becomes fixed. It you are called on to examine a knee injury and you respond by saying "pack in ice until morning," the next time the trainer or coach has to manage this injury he will "pack it in ice" himself. Indeed, if the treatment is to be standardized into such a pattern, he is perfectly correct to do so.

It has been shown through years of observation, however, that nonsurgical treatment is not always the best treatment. Among orthopedists there may be considerable difference of opinion as to just how often surgery is indicated and just how complete the surgery should be. But I know of no one, particularly one interested in the treatment of knee injuries, who would say that surgery is never indicated. It must be admitted, therefore, that surgery is indicated for certain types of injuries.

An objective study of results shows that surgery done early, within 10 to 14 days, is distinctly more favorable than surgery done at a later time.[1b] Careful investigation of many cases has shown that the most vital single factor governing the degree of recovery from a severe knee ligament injury is not the severity of the injury, the location of the tear, or the age of the patient; it is the time at which the operation is done.[1b] Almost without exception in this long series (over 100 cases), the patient who was operated on within two weeks obtained a better end-result than a comparable patient operated on at a later time or treated nonsurgically. The patient with a mild injury, for whom indecision and procrastination resulted in considerable delay before operation was done, obtained a much less perfect result than did the patient with a severe injury, for whom operation was done promptly. The very nature of the most severe injuries made decision to operate easy, and the operation was carried out immediately. These patients, in spite of the major injury, obtained excellent results, much better results than those obtained by patients who were less severely hurt, for whom the operative indication was not so clear and surgery was postponed or not carried out at all.

If we are prepared to concede, first, that there will be some cases in which surgery will be indicated and, second, that surgery is much more successful if done early, it must follow that the decision as to whether a patient is to be given surgical treatment must be based on early, thorough, careful examination, with the patient under anesthesia if necessary. All knee injuries must not be treated alike if the best results are to be obtained. Therefore, diagnostic procedures must be an integral part of any discussion of surgical treatment of ligament injuries.

The fact that a high proportion of these injuries occur in young athletes serves to emphasize the importance of the above statement. The athlete must have 100% recovery, or he is no longer an athlete. The athlete demands your best effort in order to preserve his athletic ability. By the same token, every patient should have this same major effort to restore him to normal.

The following precepts are a guide in the management of knee ligament injuries:

First, the goal must be complete recovery. Experience with many cases has emphasized the importance of this concept. If the immediate decision is that recovery cannot be complete and is not even worth attempting, it is obvious that it will not be complete. If we do not aim for 100% recovery, we certainly will not attain it.

Second, avoid expediency. Particularly in the athlete there are great pressures applied to avoid comprehensive treatment. The player is anxious to return to play, and the pressures of relatives and coaches that he continue competition are real. However, in the final analysis, a temporizing attitude satisfies no one. It is important that the physician decide what treatment should be done in a given case, then see that it is done.

Third, the best treatment rather than the most convenient must be selected. It must be important to the doctor to restore the patient's activity to the level he had before he was injured. If the patient wants to play football, this desire should be considered as an important one and not casually shrugged off. Once he realizes this, the player will cooperate fully with your recommendations. Bear in mind that his career is as important to him as yours is to you. Would you willingly give up your career in medicine if this could be avoided by more careful management? It is no more fair to expect him to give up his.

Fourth, treatment must be prompt. A definite decision as to proper treatment must be made at the earliest possible moment. Surgery must not be reserved for those cases where other methods have failed. Surgical treatment is a method to be chosen on its own merits and not backed into by failure of other methods.

Anatomy

The knee joint has no basic stability inherent in its bony structure. It has neither the ball and socket of the hip nor the mortise and tendon of the ankle. The slight bony stability that exists is due to the fact that the lower end of the femur is a bipod and so resists lateral motion without actual separation of one or the other condyle from the corresponding articular surface of the tibia (fig. 1 and 2). Essentially this stability is obtained by the complete investiture of ligaments which surrounds the joint and prevents separation of the femoral condyle from the tibial plateau. The medial and lateral collateral ligaments which become continuous with the posterior ligament behind and the patellar retinaculum in front serve to give this added stability. The posterior ligament which is tight only in complete extension prevents hyperextension of the knee and supports lateral stability when the knee is in complete extension. In order to permit flexion of the knee, the anterior ligament is attached to the quadriceps' mechanism, which permits motion under constant tension. The thickening of the ligamentous structures which make up the medial and lateral collaterals serves to give lateral stability. The anterior and posterior cruciates prevent anteroposterior displacement of the tibia on the femur. Each of these ligaments has its essential function and the function of each is supplemented by the other ligaments. The integrity of the knee is entirely due to the ligamentous support which it receives. Hence a ligament injury is doubly significant in the knee since the osseous portion of the joint does have so little inherent stability.

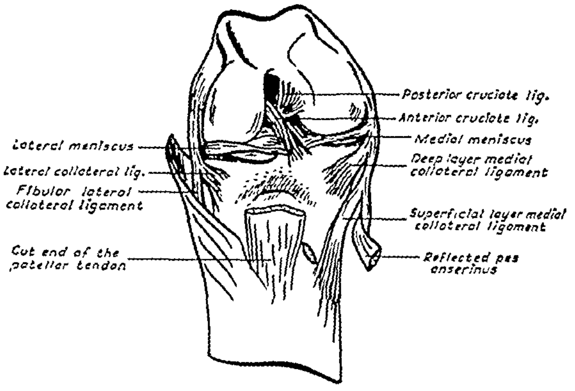
Posterior cruciate lig.
Anterior cruciate lig.
Medial meniscus
Lateral meniscus
Lateral collateral lig.
Deep layer medial collateral ligament
Fibular lateral collateral ligament
Superficial layer medial collateral ligament
Cut end of the patellar tendon
Reflected pes anserinus

Fig. 1.—Front view of knee with thigh flexed at 90 degrees. Note two layers of medial collateral ligament. Note also that medial meniscus is firmly attached to it.

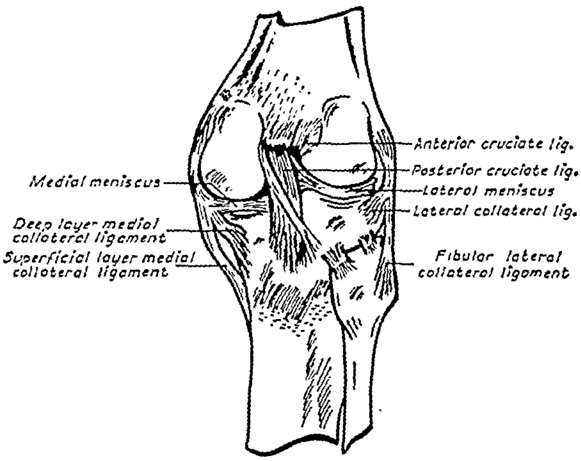
Anterior cruciate lig.
Posterior cruciate lig.
Medial meniscus
Lateral meniscus
Lateral collateral lig.
Deep layer medial collateral ligament
Superficial layer medial collateral ligament
Fibular lateral collateral ligament

Fig. 2.—Posterior view of knee in 180 degrees extension. Note that lateral meniscus is not attached to lateral ligament and that posterior cruciate is tight in extension.

The cause of a sprain is an abnormal motion of the joint which throws a stress on the ligament designed to prevent this motion. Forcing motion beyond its normal limit will result in some degree of injury to the ligament primarily involved. In the knee joint, this motion may be in any direction; adduction or abduction, overextension, internal or external rotation, forward or backward displacement, or almost any combination of these, although certain particular combinations are much more frequent. Much depends on an accurate diagnosis of the nature of the injury. Knowing the manner of injury certainly can give a lead as to the type of ligament damage to be expected. In one classic injury, the foot is fixed to the ground, the thigh rotates inward and the leg outward; the knee is forced inward toward the opposite leg and the stress is primarily received on the ligaments on the inner side of the knee (fig. 3 and 4). This is by far the most common type of the athletic injury of the knee. Using this type as an example, what may we expect in the way of injury, provided it is known that this accident occurred by the familiar lateral blocking (fig. 3) or by the "cut back" motion of the running athlete? As the foot is forced into external rotation, stress comes against the medial collateral ligament of the knee, the superficial layer of which takes the strain first. As this stretches, tears, or gives way, the force reaches the deep layer, to which is attached the medial meniscus. If the force continues, the anterior cruciate receives the stress and it too may give way, and in severe injuries the posterior cruciate may also rupture. These injuries are shown in the accompanying illustrations. Obviously, the injury may stop at any point in this progression of events. In a similar manner, adduction or internal rotation puts the force against the lateral ligament of the knee, the lateral cartilage, and the anterior and posterior cruciate. So also hyperextension at the knee throws initial stress on the posterior ligament of the joint, followed by stress against the posterior cruciate ligament and the cartilages. Direct forward motion of the tibia on the femur will injure the anterior cruciate, while the opposite force will damage the posterior cruciate.

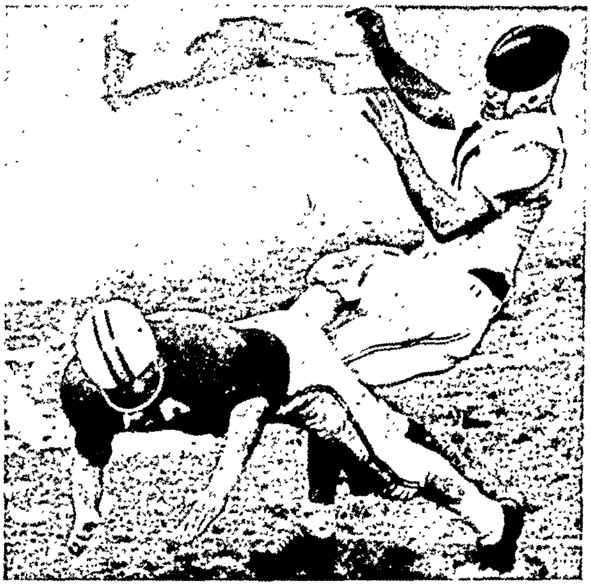

Fig. 3.—Note force applied to lateral side of knee. Cleats are fixed to ground, leg is forced into external rotation and abduction; knee opens up on medial side and tibia is forced forward in relation to femur, tension being placed on medial collateral and anterior cruciate ligaments.

Diagnosis

To consider the diagnosis of injury to the joint, what are the important factors? First a general evaluation of the situation: Did it seem to be a serious injury? Was the player immediately disabled, or was he able to keep going? Did he feel that he had a serious injury? Was he able to come off the field under his own power, or was he carried? Was he suffering extreme pain, or was it relatively mild? After this evaluation, an early, careful, and complete physical examination of the joint is of major importance. The earlier this can be done the better, since often elements can be noted early which become obscure after pain and swelling screen the symptoms. Note whether tenderness is at the joint line, above the joint, or below. Check the knee carefully for abnormal mobility in all directions, including rotation, lateral motion, and anterior and posterior motion. Observe the degree and rapidity of the swelling. Investigate whether the knee was actually locked at the time of injury or whether it is actually locked at the time of the examination. All of these things are of extreme importance if they are done in the early stage before pain, swelling, and apprehension become factors. Often, in this initial examination, a definitive diagnosis as to the location and extent of ligament injury can be made.

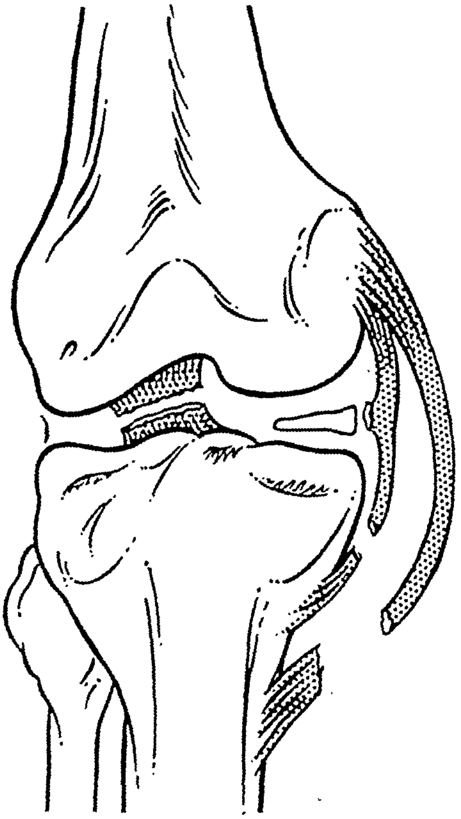

Fig. 4.—Classic injury resulting from forces shown in figure 3. Note superficial layer and deep layer of medial collateral ligament torn near tibial attachment. Medial meniscus is ruptured and anterior cruciate ligament has torn completely.

The injury must be classified as to severity as well as location. The simplest classification of knee ligament injuries is into three divisions: mild, moderate, and severe.

Mild Injury.—In a mild ligament injury, we postulate that there has been some damage in the ligament but that its strength has not been materially impaired. The symptoms of such an injury are tenderness at the site of the tear; pain on active use of the knee; local swelling at the site of the injury; pain on forced motion or attempt to duplicate the motion which caused the damage. The negative findings which are important in diagnosis of a mild injury would be no instability, no blood in the joint, no effusion in the joint, no locking of the joint, and no pain on ordinary motion of the joint.

Provided that determination can be made that it is a mild injury, treatment can be based on the premise that the ligament is actually intact. This type of ligament injury where prolonged and extensive treatment is not necessary fortunately includes the great bulk of ligament injuries. The basis of treatment is (*a*) protection against further injury and (*b*) relief of local symptoms by injection into the involved ligament some of the various substances such as procaine, hyaluronidase, or hydrocortisone. With this injury, activity can be resumed at once or at least relatively soon, but active sports should not be permitted immediately after local anesthesia. Complete immobilization is neither necessary nor desirable. The patient may be rapidly rehabilitated without danger.

Moderate Injury.—In the second group, the moderate ligament injuries, it is considered that the ligament has been partially torn, rather than just having had a few fibers of the ligament pulled apart or separated. A certain definite portion of the ligament has been damaged and its strength impaired. It may be 10 to 90% ruptured. The symptoms here are similar to those of the mild injury only greater in degree. Each of these groups shades imperceptibly into the other. The positive findings are pain in the knee; tenderness at the site of the injury; disability of a greater degree than in the mild type; swelling at first localized at the area of damage, followed by swelling diffusely about the joint; fluid or blood in the joint; pain or reproduction of the force and direction of the injury; and possibly locking due to cartilage damage. There is no abnormal motion either laterally or in anteroposterior displacement of tibia on femur. Findings indicating complete avulsion of a ligament should not be present if the damage to the ligament is only partial.

The treatment of moderate sprain is based on the premise that there has actually been significant damage to the ligament with weakening of its structure and considerable loss, or at least potential loss, of function. Therefore, it must be more comprehensive than in the mild group. Treatment consists of rest, local injection, compression bandage, cold pack early, followed by heat, later protection by splints, pressure dressing, and aspiration of the joint. This must be followed by a period of rehabilitation, the rehabilitation being necessary since there is a required period of immobilization during the course of treatment. In rehabilitation, active physical therapy, increasing active use, protective strapping, and reeducation are all of considerable importance. This group of ligament injuries is the one where injudicious overuse or too early return to physical activity may make the difference as to whether or not recovery is prompt and complete. Reduction of pain and swelling by local injection must not be permitted to cover up the true nature of the injury since active stress must not be allowed until healing is complete. Ordinarily recovery should be expected, with no residual disability in the joint. By far the major number of knee ligament injuries will fall in the first and second groups.

Severe Injuries.—In consideration of the third group, the severe ligament injuries, diagnosis is based on the premise that one or more of the major ligaments of the knee is completely torn loose from its attachment, or torn through its substance. The mechanism of this injury is that previously mentioned, namely, forcing the knee through a wide range of abnormal motion beyond the tolerance of the ligament. The symptoms in this type of injury are much more severe. Examination and evaluation reveal immediate disability; giving away of the knee joint; severe pain in the knee and leg; definite abnormal motion (may be rotatory, lateral, or anteroposterior); instability of the knee joint; blood in the joint; blood infiltrating through the tissues; local swelling first at the site of injury and very rapidly into the knee itself; locking, which may or may not be present; and confirmatory x-rays showing abnormal lateral motion at the knee joint (fig. 5).

The treatment of this serious type of ligament injury is extremely important and this is the field where there has been some difference of opinion as to the best measures to be employed. Fortunately, this type of injury is not common, but, when it does happen, it can be disabling to the point where the athletic career is abruptly terminated.

If at all possible the diagnosis must be made at once. If one waits three or four weeks until swelling and pain subside instability becomes quite obvious. The optimum time for treatment has passed. Diagnosis must be early and definitive in order to permit the proper decision as to treatment.

Once the diagnosis of a complete ligament tear has been made the method of treatment must be elected. It will not suffice to try so-called conservative treatment first and then proceed to surgery. Early repair yields so much better and surer results than late repair or reconstruction that surgery must not be reserved for those cases in which conservative treatment has failed. Modern anesthesia, operating room asepsis, highly skilled personnel, and antibiotics have minimized the hazards to the degree that in the well-run hospital with a competent surgical team, open surgery can confidently take its place alongside nonsurgical measures. In the absence of complicating factors the management chosen must be that method which will give the highest percentage of the most complete recovery and in the shortest time.

I believe that if one can demonstrate complete severance of any single ligament or of any combination of ligaments of the knee surgical repair is mandatory. The repair should include not only one ligament but all ligaments involved. It makes little sense to go to the trouble of repairing the collateral ligament and ignore the cruciate because it "adds to the severity of the operation" or is "too difficult" or "may not be essential." The cruciates are not vestigial. One has only to examine the splendid mechanism of the anterior cruciate, to note its size, to check its strength, and to recognize its vital structure in order to realize that this is not an evolutionary misfit ready for the discard. The cruciates play a living vibrant part in that ingenious mechanism that is the knee. We may argue about their exact function but be assured they have a major one.

Even though we agree that the knee has many interlocking ligaments and that it acts as a physiological unit and that it may spare some portion of that unit without disaster, the very fact that the cruciate is one of those factors means that the knee is actually or potentially less than normal without it. The cruciate should be repaired since in no other way may a normal knee joint be attained.

I examine many knees in which the only detectable complaint is cruciate instability. These patients seek treatment because to them the condition is materially disabling. This in itself is evidence that the cruciate in a given case may be vital for adequate function.

Late cruciate reconstruction is highly speculative and should be done only when the stakes are high, as, for example, a professional baseball player who is unable to play because of anteroposterior instability. Early cruciate repair is highly successful and should be done as a matter of course. It is not unduly technical and any competent orthopedist can do it if he properly prepares himself in the necessary technique.

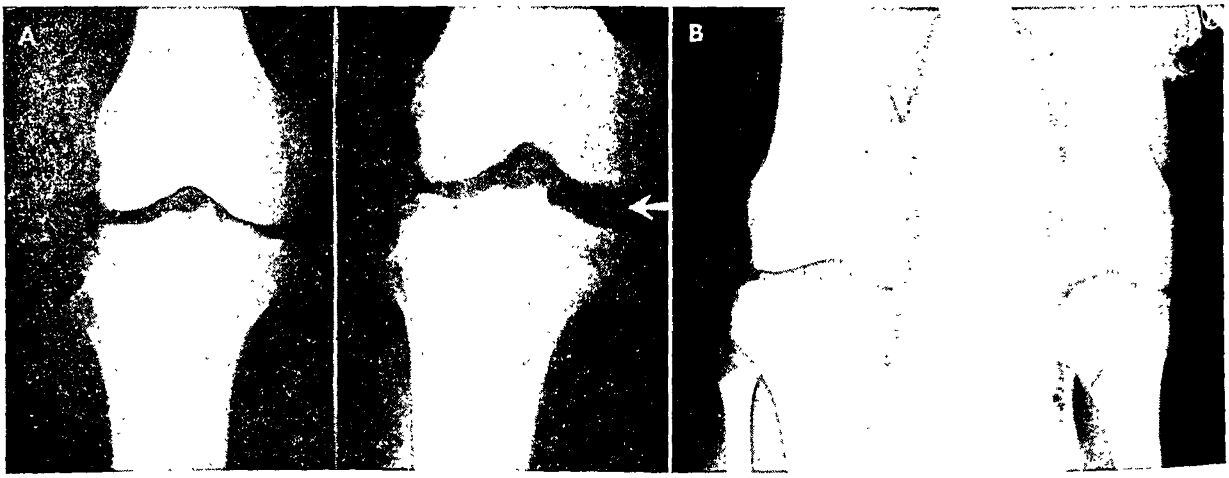

Fig. 5.—*A*, x-ray of injury to medial collateral ligament of knee: *left*, normal anteroposterior view; *right*, position of abduction of leg on thigh; arrow indicates increased tibio-femoral point space. *B*, x-ray illustrating damage to lateral collateral ligament: *left*, straight anteroposterior view of knee; *right*, with leg adducted on thigh.

In certain cases the ligament may repair spontaneously, especially the collateral ligaments. The danger is in our inability to determine short of surgery which case will heal with normal length and which will not. I have actually found at surgery the tibial end of the medial collateral lying in the joint on top of the medial meniscus (fig. 6). I have seen the ligament torn with the ends free and the tendon retracted an inch or more (fig. 7). I have located the femoral attachment of the medial collateral ligament lying in the joint on top of the meniscus (fig. 8) with the femoral end of the posterior cruciate lying over the medial meniscus. There are many other such situations which are unredeemable except by surgery. With such pathology actually seen, one becomes very skeptical of uniformly good results reported from nonsurgical treatment.

What about results of surgery? After a survey[1b] of 80 consecutive cases of ligament injuries the findings showed that, regardless of the severity of the injury, early repair gave approximately 90% of good results (over 90% in athletes). The time and the completeness of repair were much more important than the nature or severity of the injury. Failure of the cruciate repair was the biggest single cause of permanent disability in knee ligament injuries. Repair of the cruciate was highly successful early but very unpredictable late.

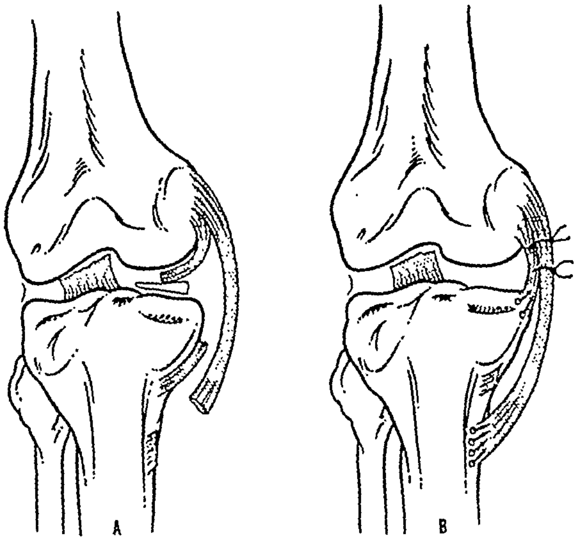

Fig. 6.—Injury from rotation-abduction force, before (*A*) and after (*B*) repair. Note deep layer of medial collateral ligament torn from tibial rim and from cartilage and lying on top of cartilage, requiring surgery for deep layer to be repaired. Note femoral attachment of anterior cruciate avulsed and widely separated.

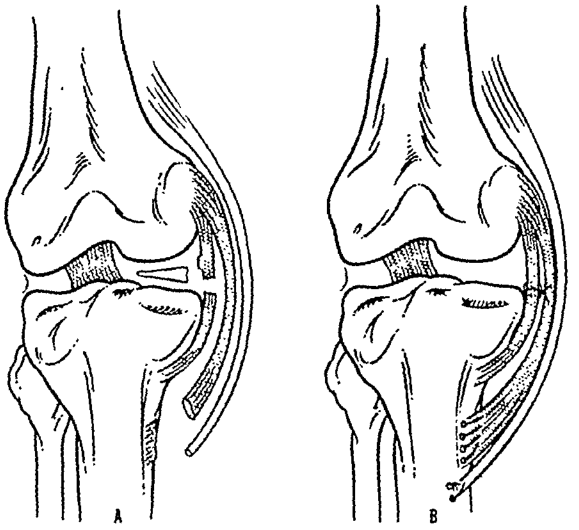

Fig. 7.—Classic injury of semitendinosus tendon attachment pulled loose, with wide separation of ligament attachment, before (*A*) and after (*B*) repair.

Bennett[2] lists four musts for the surgical treatment of knee ligament injuries: 1. The patient must be seen early. 2. The surgeon must be a good diagnostician and able to identify ligament injuries. 3. The surgeon must have good judgment. 4. The surgeon must be competent. Certainly these are not unattainable goals for the present-day well-trained orthopedist.

Management of Severe Ligament Injury

Let us consider the actual management of a severe ligament injury. In diagnosis, much depends on patient cooperation, so gentle hands are an asset indeed. Usually one finds immediate disability, often severe, knee "giving away," severe pain, blood infiltration with or without blood in the joint, "doughy" swelling, tenderness, diffuse with local areas of increased tenderness corresponding to the location of the tear or tears. Above all, one finds instability corresponding to the ligament involved. In order to determine this instability the good knee is examined first and a base obtained. Each motion in the injured knee is carefully compared with that of its fellow. The knee is checked in complete extension for adduction and abduction; then flexed to 150 degrees and abduction, adduction, and internal and external rotation are tested; then flexed to 90 degrees so the drawer sign cannot be elicited.

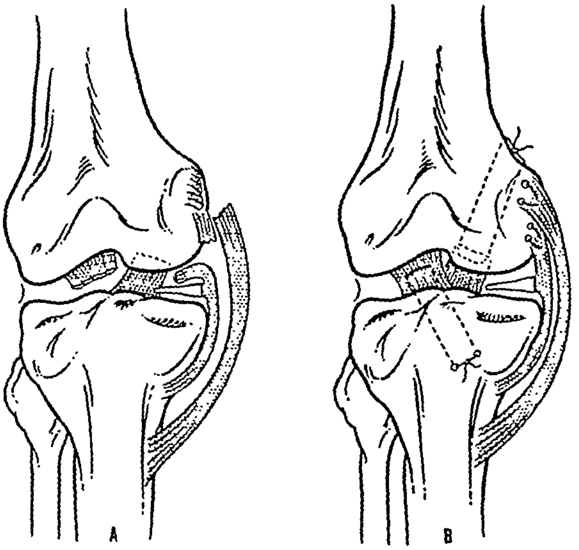

Fig. 8.—External rotation-abduction injury, before (*A*) and after (*B*) repair. Note tibial attachment of anterior cruciate torn loose and separated; femoral attachment of posterior cruciate pulled away; both layers of medial collateral ligament torn away from femoral condyle; deep layer folding inward and lying on top of cartilage. Note anterior cruciate was fastened to tibia, posterior cruciate fastened to femur. Medial collateral was pulled away from joint and attached to femur.

Twenty-five per cent of my cases of cruciate severance were not definitely diagnosed before anesthesia.[1b] After this careful examination, decision is made as to the treatment. If one can demonstrate complete severance of any ligament, surgery is advised. The exact details of surgery for repair of various ligaments to the knee have been thoroughly described elsewhere and need not be repeated here. The thing with which I am vitally concerned in this discussion is the indication for surgery, not the technique. After surgery, a heavy posterior long leg plaster splint is applied, care being taken to support the extremity by the foot and thigh, rather than beneath the calf, in order to avoid stress on the anterior cruciate ligament due to lifting the tibia forward on the femur. After this first splint has set a lateral stirrup is applied.

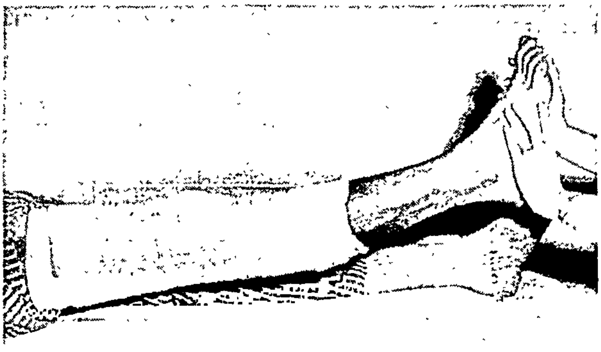

Fig. 9.—Completed cotton cast, splint being pressure bandage consisting of multiple layers of sheet wadding followed by yucca board for stability. See Campbell's "Operative Orthopedics" (edited by J. S. Speed, ed. 3, St. Louis, C. V. Mosby Company, 1956, vol. 1, p. 88) for complete details.

After the patient has returned to bed, the leg is elevated on pillows or a sling and carefully watched for circulatory impairment. The dressing is split before tightness becomes a problem and tightened up as the swelling subsides. At two weeks, this splint is carefully removed and again care is taken in the case of the anterior cruciate repair to support the extremity by the thigh and foot and not by the calf. Stitches are removed. The knee may be aspirated and hydrocortisone (Hydrocortone) or prednisolone (Hydeltra) injected if indicated by the presence of the effusion. This is not ordinarily necessary.

A very light weight long leg plaster cast is then applied with the knee fixed at 160 degrees. Frequently a walking heel is used if the repair seems stable and the patient is reasonably agile. He may use the heel for weight-bearing but is advised to continue use of crutches. At the end of two weeks in the solid cast, four weeks postoperatively, this cast is removed and a cotton cast (yucca boards over sheet wadding) applied (fig. 9). Aspiration and injection are repeated if indicated. This splint is removed in two weeks (six weeks postoperatively) and an elastic bandage utilized as indicated. If effusion persists, repeated aspirations and injection may be necessary. This is not usually necessary. Most cases do not require even one aspiration.

For rehabilitation, quadriceps setting and straight leg raising of both legs are encouraged from the first day. Patient is in a wheel chair 24 to 48 hours postoperatively. He should be able to raise the leg actively, splint and all, by 48 hours, and to walk on crutches in three to five days. Weight-bearing is not permitted, however. After the solid cast is applied (two weeks postoperatively) the patient may walk with crutches on a walking heel if progress is good. He is permitted to discard his crutches if he feels able to walk around the house without them, but in general he should use his crutches while away from home. Meantime exercise of all other available muscles is encouraged.

After he goes into the cotton cast (four weeks postoperatively), he is urged to walk, preferably without his crutches, and to continue his exercises. At six weeks the cotton cast is removed and quadriceps rehabilitation begins in earnest (see table) and continues until the circumference of both thighs is equal. Specific written instructions with definite exercises are important. The actual level of activity varies much with the individual patient. The agile, wiry type of person, relatively light weight, may be allowed more freedom than the heavy lumbering giant whose ligaments are normally relaxed in all his joints. Running is permitted as desired if synovitis permits. No contact sport is allowed until four months, and not then if the quadriceps is not completely rehabilitated.

Rehabilitative Exercises to the Quadriceps Muscle After Knee Injury or Operation

Sit on the side of the table with the legs hanging over in a vertical position.

Raise the foot on the involved side to the horizontal position slowly to the count of 3 seconds.

Hold in horizontal position to the count of 3 seconds.

Lower slowly to the count of 3 seconds.

Rest for the count of 3 seconds.

Repeat this 10 times. Rest a little.

Do this through 3 series of 10 times each, i.e., 30 times total.

These exercises should be repeated two or three times a day depending on tolerance.

When able to complete the series of 30 elevations, add weight to the foot at the next period of exercise increasing its use until it can be used the full 30 times.

Continue these exercises, adding weight successively according to tolerance until possible to raise 25 or 30 lb. through this series. Use opposite knee for control to get some idea of how much weight injured leg should be expected to raise.

Make a chart for daily progress and record on it each period of treatment, noting the ascending curve of weight-lifting capacity.

Continue exercises until circumference of involved thigh is same as uninjured thigh and until injured leg is able to raise as much weight as uninvolved side. As strength increases, these exercises can be supplemented by other exercises, such as going up and down stairs, partial knee bends, single knee bends.

Naturally, each case must be strictly individualized both as to type of repair used and as to postoperative management. A patient with a good tight repair with strong ligament fibers can be permitted more liberty. Some patients need to be pushed in their rehabilitation (for example compensation cases and females). Other cases must be held down (for example 16 to 18-year-old athletes). The elastic bandage should be discarded early in the timorous and retained as a reminder in the overbold. If effusion persists, the usual treatment is followed: aspiration, repeated as required with injection of hydrocortisone, and use of elastic bandage as long as effusion is notable.

Such a regimen carefully followed with early examination, prompt decision, and complete repair of all torn ligaments, followed by conscientious rehabilitation, will give increasingly gratifying results in treatment of major injuries to the ligaments of the knee.

In my series of over 150 cases, 80% were under 25 years of age and 55% under 20 years of age. Since so many of these cases occur in young people, one must be particularly on the alert to try to reach the goal of the best recovery of function in the shortest time.

Lee at 10th Street (3).

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MANAGEMENT OF ANKLE INJURIES SUSTAINED IN SPORTS

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Inexact diagnosis and inappropriate treatment of ankle injuries can lead to serious disability. Decisions regarding them should be left to a physician whose authority should not be questioned. The patterns of fracture of the malleoli as seen in anteroposterior roentgenograms can give valuable information about concomitant rupture or avulsion of ligaments. If advantage is taken of the 20 to 30 minutes after injury before edema, hemorrhage, and spasm occur, closed reduction of even grossly displaced fractures can sometimes be accomplished with almost no discomfort. If roentgenograms indicate that soft tissues are ruptured or trapped between bony parts, prompt surgical correction is indicated. Cold, compression, rest, and elevation are the four basic elements of treatment for minor injuries. There is no justification for the use of procaine as an immediate therapeutic agent in any athletic injury. Operation was necessary in the case here described, but active motion without weight-bearing was started at 3 weeks, weight-bearing was permitted at 15 weeks, and skiing was resumed at 18 weeks after the injury.

The doctor who assumes responsibility for a group of athletes is in a unique position to study trauma. Circumstances are ideal for observation of injury from the moment of occurrence to full recovery. In sports involving quick pivoting on a fixed foot, such as football, soccer, and basketball, or unanticipated wrenching with a lever as in skiing, a high proportion of these injuries will involve the ankle.

The incidence of injury can, of course, be reduced by physical conditioning and the acquisition of skill in the techniques of the sport. It is a truism that the outstanding athlete is rarely injured, and then only under unusual circumstances. But not all participants in active sports are neuromusculoskeletal geniuses, nor do they have the time to become technical virtuosos.

For these, a considerable measure of protection is afforded by regular use of ankle wraps.[1] Applied over the inner of two pairs of socks, with a turn around the heel (fig. 1), these nonelastic bindings, which the player applies himself, effectively limit lateral mobility without interfering with flexion or

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extension. When required of all players at all practice sessions and games, the incidence of ankle injuries can be reduced at least 50%.[2]

Despite conditioning, ankle wraps, and skillful coaching, ankle injuries still occur, and the doctor's duty begins at the moment of injury. He should himself go on the playing field and decide whether the injured player should continue play or leave the game, and, if he leaves, whether he should walk or be carried. To leave such decisions to a coach or trainer is to gamble with future disability with the cards stacked against the player. The doctor's authority in these and other medical matters should be absolute and unquestioned. Practically all coaches today are quite happy to be relieved of this responsibility. They have enough difficult decisions in their own field.

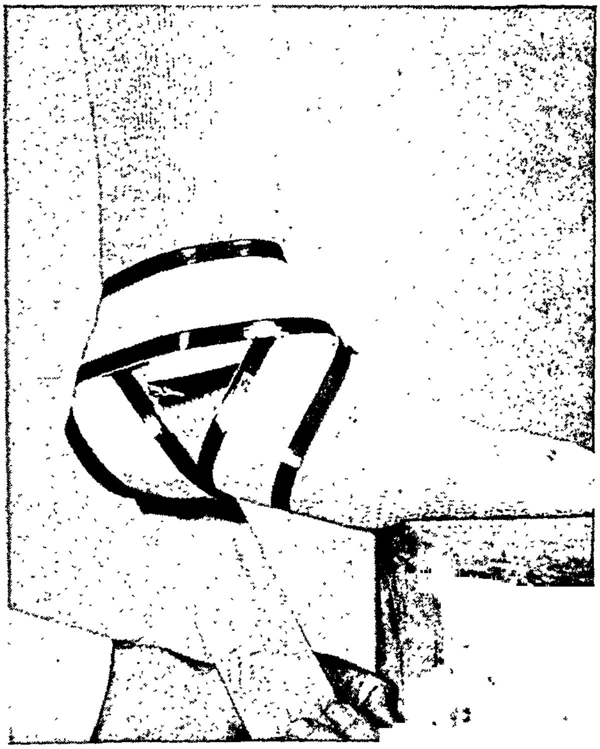

Fig. 1.—Nonelastic protective ankle wrap in process of application. Edges of wrap have been darkened to show basic turns of bandage. Turns around heel limit lateral mobility without interfering with flexion and extension.

Once off the playing field a preliminary survey can be made. All that can be accomplished at this time is differentiation between major and minor injury. Minor injury means sprain or incomplete rupture of ligament; major injury means fracture, complete rupture of ligament, or both. Almost invariably, anteroposterior and lateral x-rays will be necessary. Even the most experienced examiner cannot be certain of the presence or absence of fracture or widened joint mortise by examination alone. It is better to take 50 negative x-rays than to miss one serious injury.

Accumulated evidence from observation of the mechanism of the injury as it occurred, the location of pain, tenderness, and swelling on examination, the type of fracture, and the state of the joint mortise from the x-ray should be enough to establish a precise diagnosis of major bone and ligament injury. Fracture is, of course, obvious in the x-ray films, but the diagnosis of complete ligament rupture can be more subtle and, if not recognized, can be at least as serious as fracture in terms of future disability. For practical purposes, only three ligament complexes need be considered: the medial collateral (or deltoid), the tibiofibular-fibulotalar, and the lateral collateral (or fibulocalcaneal).

Most severe ankle injuries sustained in sport are of the abduction–external rotation type, in which the talus twists and pries the fibula from the tibia. Either the fibula itself fractures or the anterior tibiofibular ligament ruptures, producing widening of the tibiofibular syndesmosis (fig. 2). In either event, as force continues, the deltoid ligament gives way (or, more rarely in young men, pieces of the medial malleolus of varying size are avulsed) and the joint space between the talus and the medial malleolus can be seen to be wider than the horizontal component of the ankle joint.

Fracture accompanies ligament rupture more often than not, and the type of fracture, as Lauge-Hansen[3] has pointed out, is a most valuable key to diagnosis. Internal rotation-adduction forces can stretch only the fibular collateral ligament, the others being compressed, and then only if the characteristic horizontal avulsion fracture of the lateral malleolus does not occur (fig. 3). Isolated injuries to this fibulocalcaneal ligament, even when severe, only rarely require primary open surgical repair.

Analysis of ankle injuries sustained in sport should not require much time, and often advantage can be taken of the 20 to 30 minutes after injury, before edema, hemorrhage, and spasm occur, during which nature imposes analgesia, to accomplish closed reduction of even grossly displaced fractures with almost no discomfort.

For external rotation-abduction injuries in which the medial malleolus is intact, the simple device of suspending the stockinette-encased limb has proved most helpful (fig. 4). With the gastrocnemius relaxed by flexion of the knee, the ankle naturally falls into adduction, moderate flexion, and supination, reversing the mechanism of injury. Often little or no manipulation is required to achieve excellent reduction of grossly displaced fracture (fig. 5). Doughnuts of felt or foam rubber are applied over the malleoli and held with sheet wadding before plaster is applied. Most ankle injuries of such severity as to require splinting should be immobilized in a cast extending to the groin with the knee flexed 30-40 degrees.

Another set of x-rays is taken as soon as the plaster has set. If widening of the joint mortise is still present, it can be assumed that avulsed ligament is trapped either between the talus and the medial malleolus, in the tibiofibular syndesmosis, or both and prompt surgical correction is indicated.

Report of a Case

A 25-year-old student sustained a severe external rotation injury to the right ankle while skiing (fig. 6). Closed manipulation without anesthesia and application of a long leg plaster cast was carried out within an hour of injury. Films taken on his return to Boston five days later showed widening of the space between the talus and the medial malleolus and a high fracture of the fibula. At operation, a week after injury, the deltoid ligament was found avulsed from the medial malleolus and trapped in the ankle joint. The anterior and posterior tibiofibular ligaments were completely torn. Clot was removed from the tibiofibular syndesmosis, the deltoid ligament was sutured in proper position, and the tibia and fibula were bolted together. Active motion without weight-bearing was started three weeks after operation. The bolt was removed and weight-bearing permitted three months later. The patient skied again four and one-half months after injury.

Displaced bimalleolar or trimalleolar fractures in young athletes almost always require operation. Precise closed reduction is difficult, since no fixed point remains on which to hinge manipulation, and interposed soft tissue between the fragments of the medial malleolus is the rule rather than the exception. Little less than anatomic perfection can be accepted in these severe multiple ligament and bone injuries since these young men have at least five decades of use of their ankles ahead of them. Only the most trivial fractures, not involving ligaments, can safely be treated by a short leg boot and weight-bearing device.[4] Torsion within a walking boot can displace even the common, and usually uncomplicated, external rotation fracture of

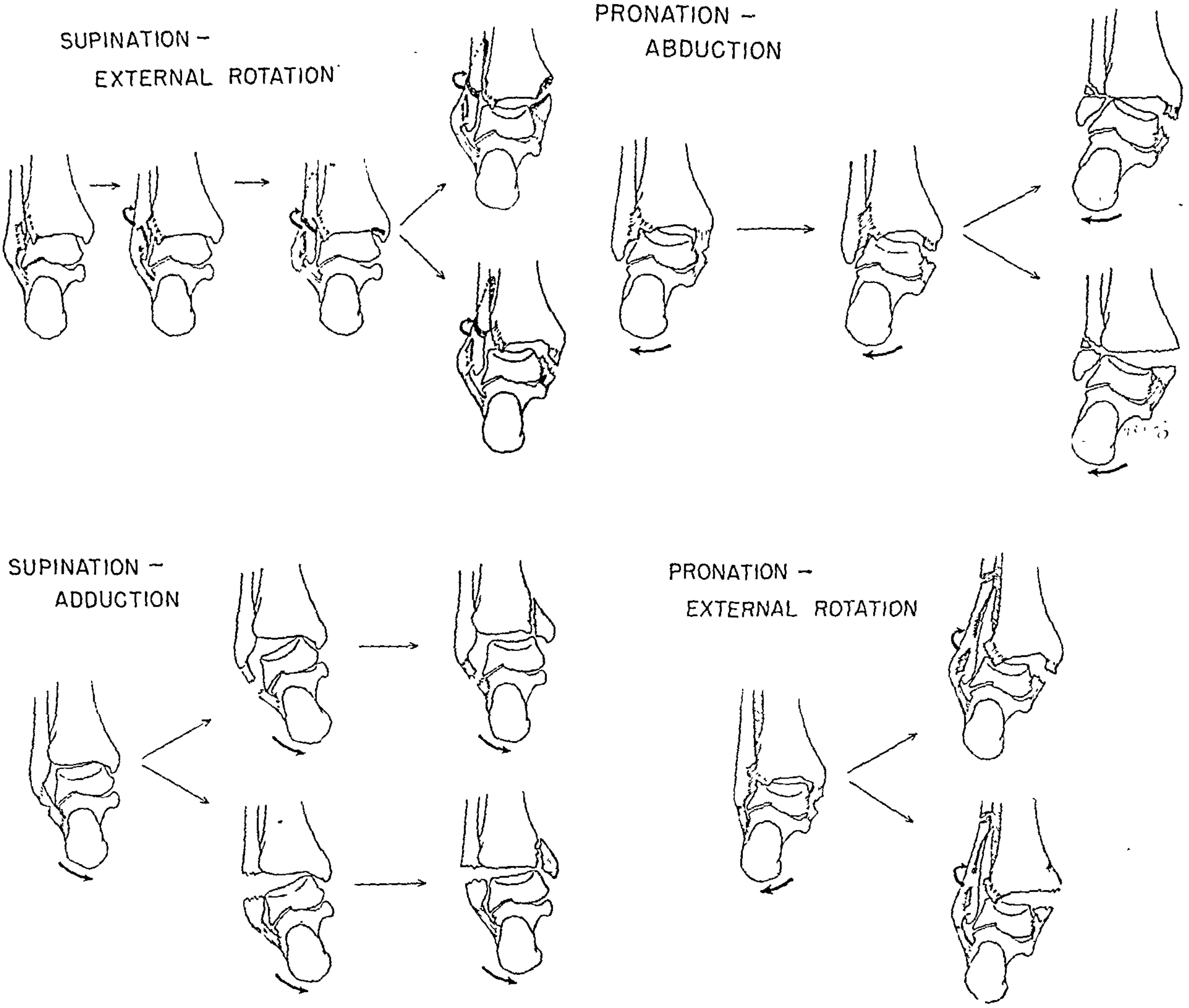

Fig. 2.—Patterns of ankle injury (after Lauge-Hansen[3]). Combinations of forces can occur but are uncommon. Fibula fracture in pronation-external rotation injuries can be in upper half of bone.

the distal fibula, since concomitant injury to the deltoid ligament can be more severe than originally appreciated.

If, at the first examination, within moments of injury, the damage is found to be minor, four principles of treatment are instituted—cold, compression, rest, and elevation. These are based on the concept that a sprain is a partial tear of a ligament, with hemorrhage at the point of tear, absorption of the resulting hematoma, and replacement of the gap by fibroblastic scar. The process is the same as the healing of any sterile wound. No method has yet been found to accelerate the process beyond nature's rate, but many are available which slow it down or disturb the end result. These include the use of procaine hydrochloride (Novocain), hydrocortisone, rough manipulation and massage, and "running it out." Cold, promptly applied, constricts the arteriolar bed and limits the hematoma. Compression disseminates the hematoma already present and speeds its absorption by

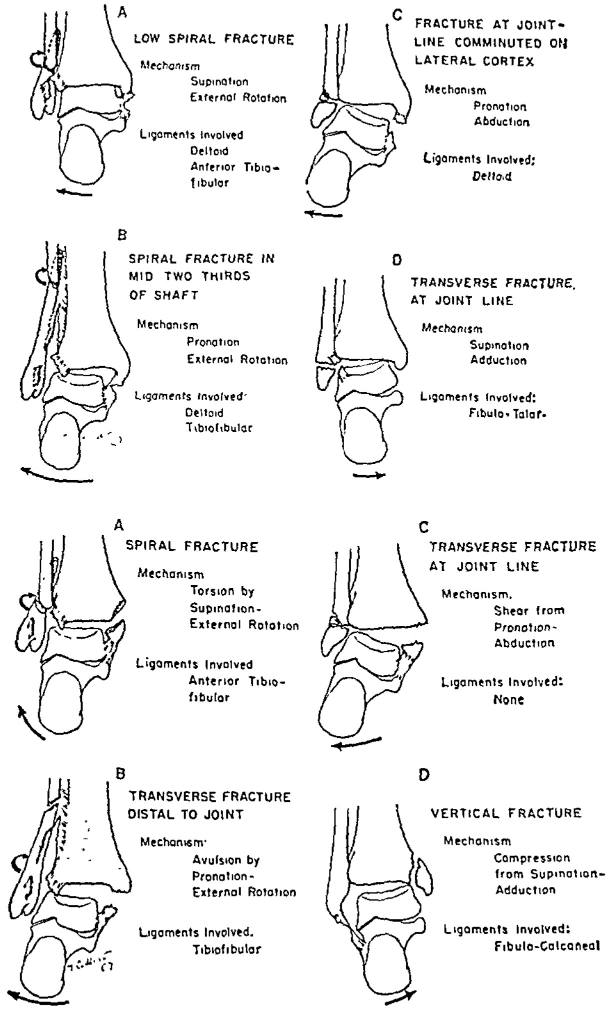

Fig. 3.—Key to analysis of ankle injuries: *top*, fibular; *bottom*, medial malleolar.

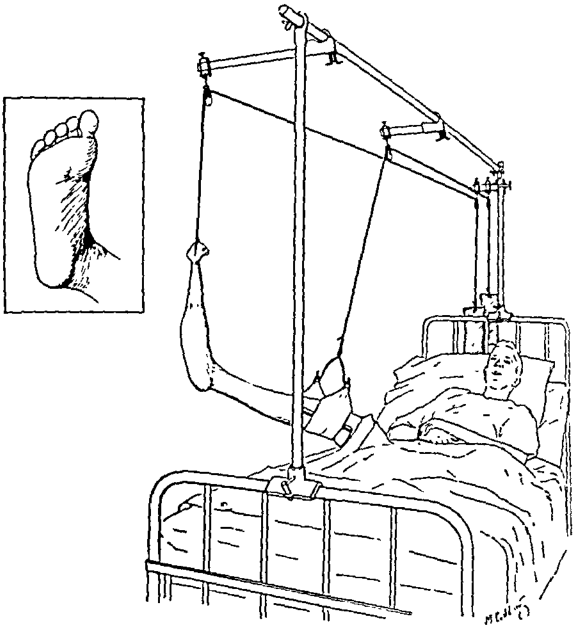

Fig. 4.—Stockinette suspension for external rotation-abduction fractures and ligament avulsions. Foot and ankle naturally fall into position which is opposite of forces producing injury. Reduction is often effected without further manipulation.

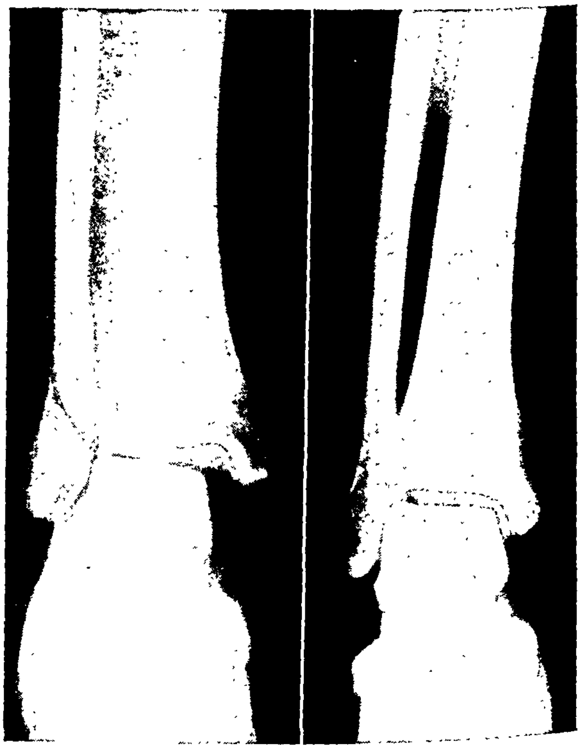

Fig. 5.—Supination-external rotation fracture of fibula with rupture of deltoid ligament before and after 12 hours' suspension in stockinette (fig. 4). Medial side of ankle was explored. Deltoid ligament was found avulsed from its distal attachment and rolled on itself but not trapped in joint.

increasing its surface area (fig. 7). Rest is obvious. As in any injury, whatever motion hurts is wrong, whatever does not hurt is right. Elevation minimizes the edema of dependency and disuse. At this first examination, when the injury has been determined to be a sprain and not a ligament rupture or fracture, a bevelled doughnut of foam rubber, of the tan open-cell type, 2.0 cm. in thickness, is placed over the injured side of the ankle with the malleolus in the aperture. The skin is protected from direct contact with the rubber by sheet wadding. The rubber is then compressed to about half its thickness with an elastic cotton bandage, extending from the toes to the upper calf. The limb is then immersed in cold water (40 degrees) or packed in ice bags for 30 minutes. The wet dressing is then replaced, crutches are fitted, and the patient is instructed in their use. He is advised to spend as much time as possible during the next 24 hours with the ankle elevated above the level of the heart.

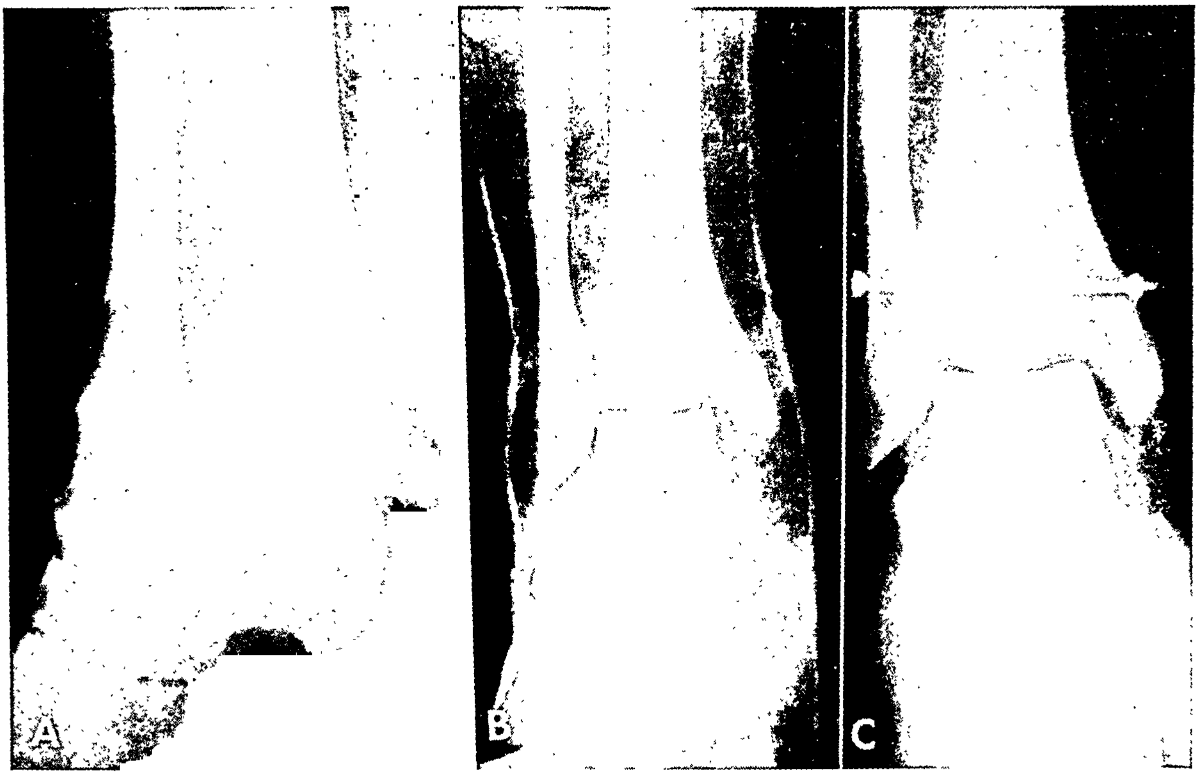

Fig. 6 (reported case).—*A*, film taken immediately after severe external rotation injury sustained in skiing. *B*, film taken five days after immediate closed reduction. Space between talus and medial malleolus is twice as wide as normal. *C*, postoperative film. Trapped deltoid ligament has been removed from joint, and joint mortise has been restored by bolt, which was removed three months later.

At the second examination, 24 hours after injury, edema should be minimal, ecchymosis may already have appeared at the periphery of the foam rubber pad, and by gentle palpation and manipulation an accurate analysis of the particular ligaments involved and their degree of involvement can be made. It is convenient to grade the severity of sprain from 1 to 4, 1 being the least degree of injury which can be classified as sprain and 4, complete rupture. Such classification is of help in prognosis, a matter of great importance to most athletes and coaches. The majority of sprains fall into grades 2 and 3. Experience during the past 70 years at the Harvard department of athletics has established that the commonest ankle injury, a grade 2 sprain of the anterior tibiofibular and fibulotalar ligaments, treated properly, with full cooperation from the patient-player, will be sufficiently healed in 8.2 days to permit full participation in contact sport. It has become equally clear over these seven decades that any prognosis ventured before the second examination, 24 hours after injury, is almost certain to be wrong.

At this second visit, it can safely be assumed that the sources of bleeding have sealed off and heat therapy, followed by gentle centripetal massage, can be started. Electronic and other complicated sources of heat have little advantage over hot water. Diathermy, in fact, is contraindicated in joint injuries since it tends to produce effusion. The psychological effect of a whirlpool bath is much greater than the massage of moving water and bubbles.

Weight-bearing is permitted as soon as natural walking is possible. When pain on manipulation and tenderness approach the vanishing point, the ankle is taped and the player is put through his paces on the playing field under the eye of his doctor, coach, and trainer. He returns to full activity only if his performance is flawless. The ankle is protected by adhesive tape, with turns around the heel to minimize lateral mobility for at least the next year for every practice session and game. The old adage "once a sprain, always a sprain" has sound basis in the fact that ligament heals with scar, which is only slowly replaced by orderly elastic collagenous tissue, and the disorganized fibroblast pattern of scar is always weaker than the tissue it replaces.

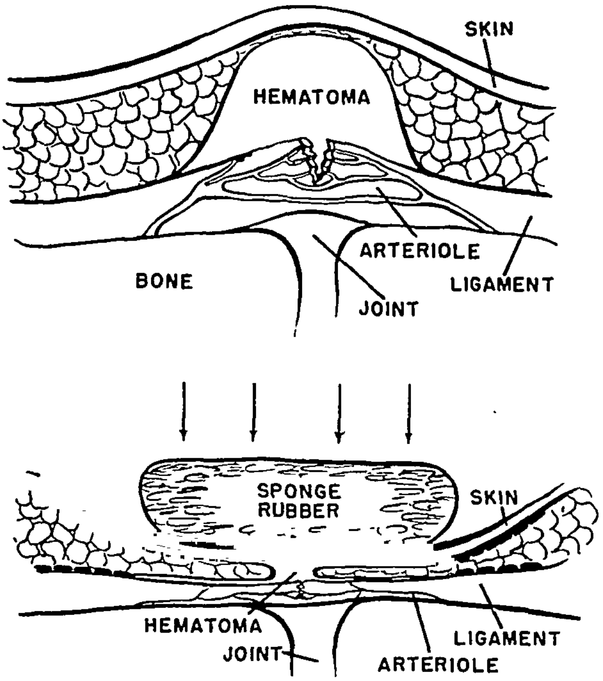

Fig. 7.—Effect of compression on hematoma accompanying a sprain. Blood is disseminated through tissue planes, increasing its surface and speeding absorption.

There is no justification whatever for the use of procaine in any athletic injury. Pain may temporarily be abolished, but performance is usually poor and further damage to the injured structure is almost inevitable. Hyaluronidase and hydrocortisone may have a place when hemorrhage is unusual in degree or sensitivity to pain high. But it must be remembered that arthrocentesis is no different from arthrotomy, from a bacteriological point of view, and a locker room is hardly as safe as an operating theater. Further, no analgesic substance should ever be injected unless it is absolutely clear that pain is much greater than the basic ligament injury usually produces.

Plaster splints are used only for severe or multiple sprains, and are removed as soon as possible. Atrophy of thigh and calf musculature can occur at a remarkable rate and can be corrected only by careful, daily, supervised, progressive resistance exercise.

Summary

A program of management of ankle injuries sustained in sport has been developed over seven decades of experience at the Harvard Department of Athletics and includes methods of prevention, prompt diagnosis, and implementation of treatment for major and minor injuries.

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EFFECTS OF IONIZING RADIATIONS ON BENIGN LESIONS.—Irradiation for benign conditions may produce tissue changes more disabling than the original condition for which the x-rays were administered. A latent period of several decades between exposure to irradiation and tissue breakdown is common. Thus, those who administer the irradiation may be unaware of the late consequences. Cancer developed in 22 per cent of the 165 cases reviewed in this study and can be predicted in others. Contrary to previous teaching, carcinoma in irradiated skin of the face is usually of the basal-cell type. The morbidity of this entity is high, but death from radiation necrosis is rare. Surgical therapy should be prompt and thorough. Prophylactic excision may preclude the ultimate development of carcinoma. Evidence gained from this study and those of others suggests that those not fully qualified in the therapeutic use of x-rays be excluded from the application of this potentially dangerous tool.—Bradford Cannon, M.D., J. G. Randolph, M.D., and J. E. Murray, M.D., Malignant Irradiation for Benign Conditions, *The New England Journal of Medicine,* Jan. 29, 1959.

low no definite calendar, and the degree and extent to which they occur vary greatly even in individuals of advanced age. Not all degenerative changes are of clinical importance, and, as McRae has pointed out, disks may bulge, herniate, or rupture without any symptoms whatsoever.

This paper is written as a contribution toward a better understanding of degenerative arthritis of the lumbosacral joint. The significance of clinical and roentgen findings to be described will be considered controversial by some. Nonetheless, I feel that a reasonable approach to the treatment of low back pain of intrinsic cause must come from a better understanding of degenerative arthritic lesions which occur in the lower lumbar region of the spine and particularly in the lumbosacral joint.

This joint, the end-space of the movable spine, is a compound articulation which consists of an intervertebral disk and two facet joints. The disk is an amphiarthrosis, a modified joint with a ball-bearing-like action. The facet joints are diarthroses or true movable articulations. The first sacral nerve root bears an intimate relation both to the disk and to the facet joints. The lumbosacral joint, subjected to the greatest amount of superincumbent body weight, is more prone to degenerative disease than any other joint in the lumbar spine. In 222 patients examined over the three-year period, 1955 to 1958, degenerative arthritis occurre ion of L-3 in 5 patients, the region of l bo-sacral region in 160, and the reg -5 in 35.

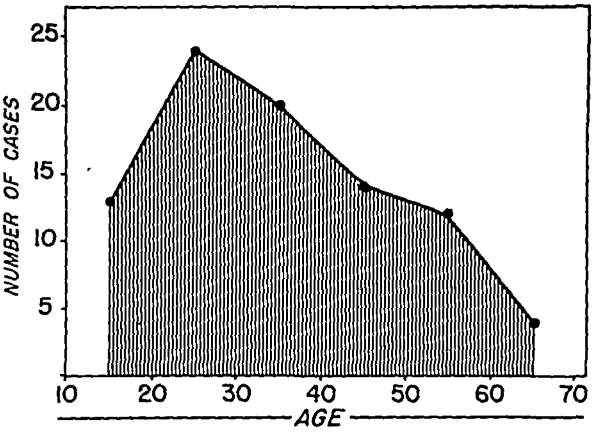

Fig. 1.—Graph showing ages of patients at onset of symptoms of lumbosacral arthritis.

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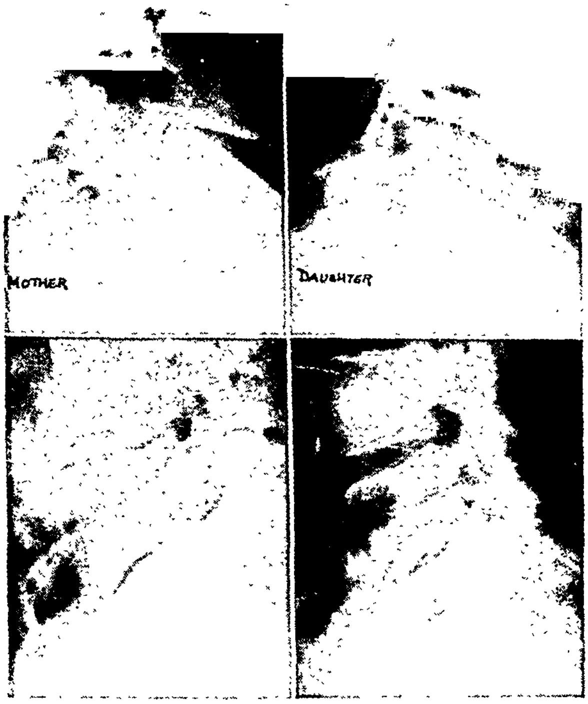
Method of Study

One hundred twenty-five patients, of whom 83 are female and 42 are male, were chosen for this study. The patients in the study, and whenever possible their families, were questioned carefully on repeated occasions in an effort to obtain histories of a high degree of accuracy. Special attention was given to the history, for prior to the first examination many had been treated for long periods of time by doctors of varying disciplines. The nature of the treatment that had been rendered and the patient's response to it efully recorded. The type, frequency, an n of acute episodes of pain were chart l differentiation between acute and ch toms has been [illegible]

Eleven patients were treated because of injuries sustained in industrial accidents. It is of interest that roentgenograms taken at the time of injury showed preexisting lumbosacral arthritis in 10 of these patients, and, therefore, their accidents were considered aggravations of an already existing degenerative disease. Included in the study are members of 10 families in whom there was definite evidence of a hereditary tendency toward degeneration of the lumbosacral joint (fig. 2).

The duration of symptoms prior to the initial examination varied from 1 to 40 years. Every conceivable type of treatment had been rendered, including heat of all kinds, medicaments too numerous to record, supports of many types, exercises, traction, and manipulation. It soon became apparent from scrutiny of histories that the type of treatment rendered in the early stages of disk degeneration seems to make little difference. Acute symptoms subsided in a few days regardless of what was done. With respect to manipulative therapy, questioning of the patients indicated that in the first years of their disease such treatment often gave relief. However, as the degenerative process of the lumbosacral joint progressed, manipulations either gave no relief or aggravated symptoms.



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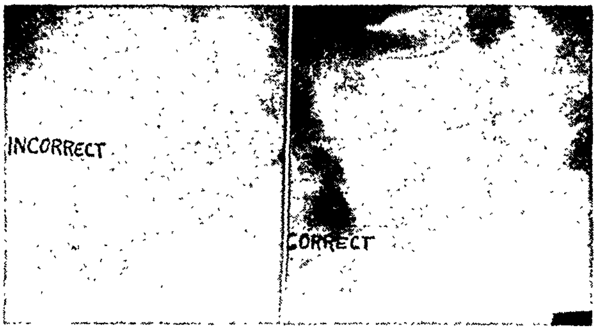

Fig. 3.—Lateral roentgenograms of lumbosacral joint in patient, emphasizing ease with which diagnosis can be missed in poorly centered film and ease with which it can be made in a well-centered film.

Regardless of whether the onset of the disease was acute or chronic, progress of lumbosacral arthritis is characterized by recurrent attacks of low back pain with or without sciatic radiation. These attacks occur at intervals of several weeks to several months. They tend to increase in severity.

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This paper is written as a contribution toward a better understanding of degenerative arthritis of the lumbosacral joint. The significance of clinical and roentgen findings to be described will be considered controversial by some. Nonetheless, I feel that a reasonable approach to the treatment of low back pain of intrinsic cause must come from a better understanding of degenerative arthritic lesions which occur in the lower lumbar region of the spine and particularly in the lumbosacral joint.

This joint, the end-space of the movable spine, is a compound articulation which consists of an intervertebral disk and two facet joints. The disk is an amphiarthrosis, a modified joint with a ball-bearing-like action. The facet joints are diarthroses or true movable articulations. The first sacral nerve root bears an intimate relation both to the disk and to the facet joints. The lumbosacral joint, subjected to the greatest amount of superincumbent body weight, is more prone to degenerative disease than any other joint in the lumbar spine. In 222 patients examined over the three-year period, 1955 to 1958, degenerative arthritis occurred in the region of L-3 in 5 patients, the region of L-4 in 22, the lumbosacral region in 160, and the region of L-4 and L-5 in 35.

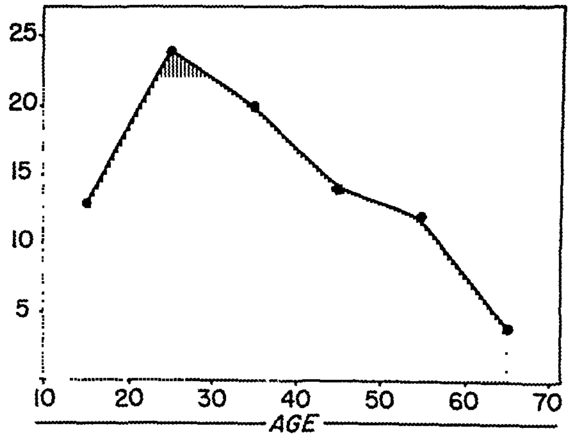

Fig. 1.—Graph showing ages of patients at onset of symptoms of lumbosacral arthritis.

The importance of the lumbosacral joint as a site of degenerative arthritis has been recognized by orthopedists generally, but this concept has been slow to extend beyond the confines of the specialty. Goldthwait,[9] in 1911, described a paraplegia which followed forcible manipulation of the lumbar spine in a 39-year-old man. The patient's signs and symptoms, viewed in light of present-day knowledge, would have indicated a diagnosis of posterior herniation of the lumbosacral disk. The catastrophic result which occurred after forcible manipulation under ether anesthesia caused Dr. Goldthwait to make extensive anatomic studies of the lower lumbar region of the spine. His article, a landmark in the recorded history of orthopedic surgery, is the first to place emphasis upon the lumbosacral joint as the site of disease which can cause pain in the lower back and legs. Prior to his article, and even subsequent to it, the sacroiliac joint, rather than the lumbosacral, has been considered the offending articulation. The concept of sacroiliac displacement as a cause of low back pain is dying a lingering death, but it is far from dead.

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My associates and I have had the unique opportunity of treating siblings and successive generations of the same family with lumbosacral arthritis. The hereditary nature of the disease has become increasingly apparent. Treatment, whether conservative or surgical, has been carried out along certain definite patterns, so that an opinion of some value can be given as to the response of these patients to the care rendered. The majority have been treated conservatively. Some have been followed for as long as 20 years. Clinical data from various age groups have been gathered and sifted. By taking a perspective in length it has been possible to record, in part, the natural history of this disease.

Symptoms in Lumbosacral Arthritis

Of the 125 patients, 87 were aware of the age at which symptoms developed. Most developed symptoms while under the age of 40 (fig. 1). Eighty-four patients were aware of the exact nature of their first symptoms. Twenty-four noted dull ache in the lower back which came on without any known cause. Forty-six had an acute attack of low back pain which resulted from a simple body motion. Fourteen gave histories of real trauma to the lower back which resulted usually from lifting weights in excess of 100 lb.

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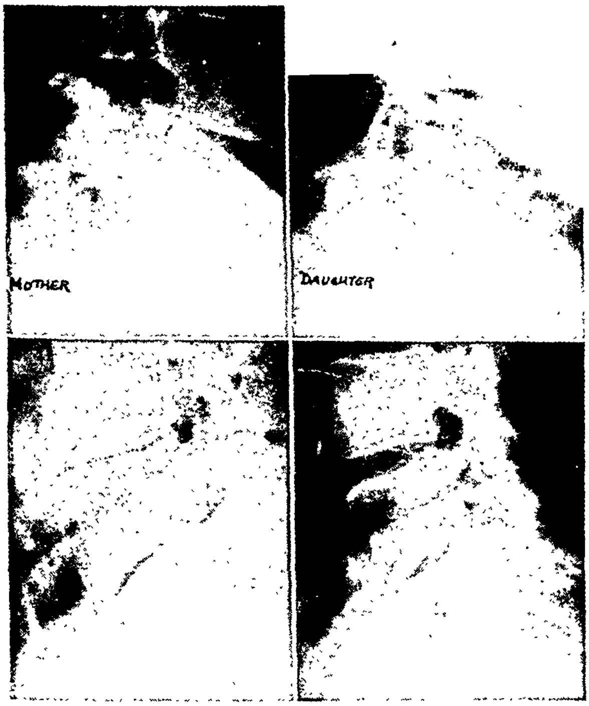

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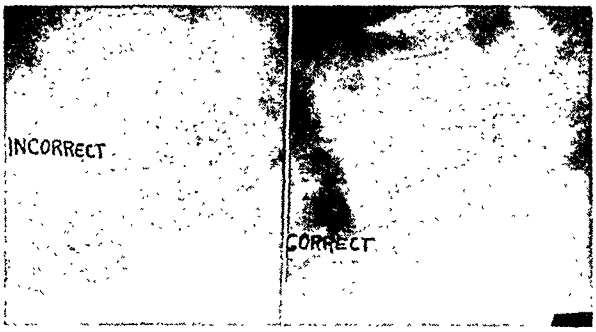

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The location and radiation of pain from the lumbosacral joint is not constant. Inman and Saunders,[9A] in 1944, pointed out that localization of pain from irritation of deeply placed skeletal structures is poor. They further demonstrated the variability in the response of deep structures to painful stimulation. Lumbosacral pain may be felt in the midline of the lower back, over the coccyx, over one or both sacroiliac joints, in the buttocks, in the lower abdominal quadrants, or in the groin. If the first sacral nerve root is irritated, true sciatic pain is felt. Unusual radiation of pain from the lumbosacral joint has led to the unnecessary removal of the coccyx and pelvic organs, especially in the female.

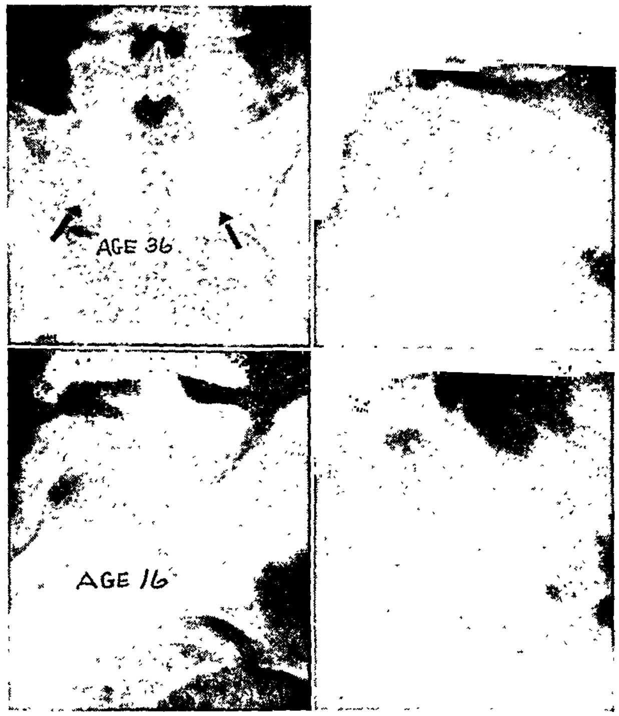

Fig. 4.—*Above,* anteroposterior and lateral roentgenograms of lumbosacral joint in 36-year-old woman. Note symmetrical collapse of disk space, lipping of anterior vertebral margins, and extreme sclerosis of superior articular plate of sacrum. *Below,* roentgenograms of lumbosacral joint of 16-year-old girl who had had symptoms for four years. Note narrowing of disk space in lateral view and loss of joint space as well as subluxation of facet joint in oblique view.

A patient examined in the acute phase of the illness demonstrates marked restriction of motion in the lumbar spine, muscle spasm, tenderness to palpation over the lumbosacral joint, and, depending upon whether the sciatic nerve is irritated or not, hamstring spasm and alteration in the achilles reflex. The signs of nerve root irritation are variable. They may be present with one attack and absent with the next. They bear no direct relationship to the degree of disk disintegration. Patients with total collapse of the lumbosacral disk space have never had leg pain, whereas others with a lesser degree of collapse have had intermittent severe leg pain.

A patient examined in the chronic phase of the disease may show surprisingly little on physical examination. Slight restriction of motion in the lumbar region of the spine and tenderness upon firm palpation of the spinous process of the fifth lumbar vertebra may be the only significant positive findings. A depressed or absent achilles reflex may be a single clue to chronic irritation of the first sacral nerve root.

The diagnosis of lumbosacral arthritis can be strongly suspected from the history and physical findings, but accurate diagnosis depends upon adequate roentgenograms. In view of the slowly progressive nature of the disease, serial x-rays are sometimes needed before the diagnosis is confirmed. Films should include standard anteroposterior and lateral views of the lumbar region of the spine with oblique views and a coned lateral view of the lumbosacral joint. Standing lateral x-rays of the lumbosacral articulation taken with the spine in flexion and extension are also helpful. The importance of accurate centering in the lateral view is especially stressed (fig. 3).

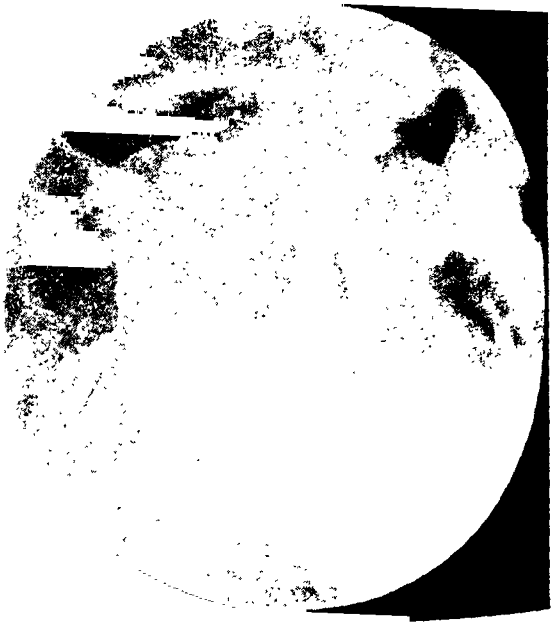

Fig. 5.—Oblique roentgenogram of facet joint at lumbosacral level in 50-year-old woman. Facets are subluxated. Superior sacral facet has impinged on pedicle of fifth lumbar vertebra to such degree that notch has formed in pedicle.

The roentgenographic characteristics of lumbosacral arthritis are demonstrated in figures 4 and 5. The progressive nature of the end-space lesion is well illustrated in figure 6.

If posterior herniation of the disk is suggested by positive neurological findings, a myelogram should be taken, provided the patient is not sensitive to iodine. In my experience, the taking of a myelogram has proved to be a procedure of low risk and high yield. No untoward results have been encountered other than headache. The electromyogram, while occasionally useful, has not proved as valuable a diagnostic aid as the myelogram.

Methods of Treatment

Eighty-three patients have been treated conservatively, and forty-two have been subjected to lumbosacral fusion. Adherence to the principle of rest has guided treatment of the acute attack. Adhesive strapping, suitable anodynes, and confinement to bed have resulted in prompt relief of acute symptoms in three to seven days. Physical therapeutic measures, including luminous heat, deep muscular massage, gentle stretching, and postural exercises, have been beneficial. A firm mattress and a bed board are indispensable. The use of a simple wedge-shaped car seat cushion can make driving for these patients a pleasure instead of an ordeal. Manipulation of any sort has been assiduously avoided.

The therapeutic aid used most frequently, both for the control of chronic symptoms and for postoperative support, has been the Goldthwait back brace (fig. 7). Made of light spring steel and covered in washed kid leather, it is comfortable to wear and is accepted without complaint by the majority of patients. The brace not only relieves chronic symptoms but it enables the patient to engage in light physical exercise without fear of an incapacitating attack of pain. Some patients in this study have worn a Goldthwait brace intermittently for as long as 20 years with remarkable relief of pain. Both backache and sciatic pain have been relieved through its use. In addition to the use of the brace, patients have been instructed in simple postural exercises. When indicated, weight reduction has been urged.

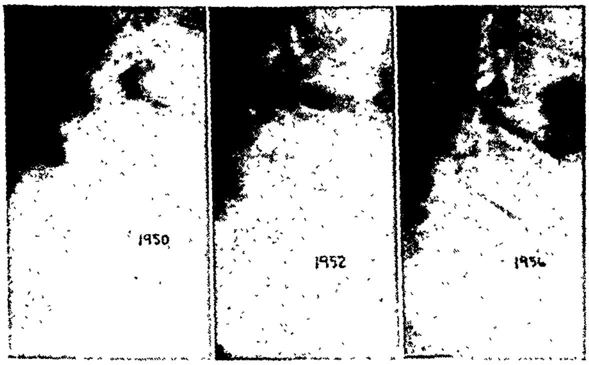

Fig. 6.—Lateral roentgenograms of lumbosacral joint of 43-year-old woman showing progression of disease over six-year period.

Of the 42 patients subjected to lumbosacral fusion, 13 had backache alone and 29 had both backache and leg pain. Of those with leg pain, 14 had posterior herniations of the nucleus pulposus. Ten of these were recent and four were older. In the remaining 15 patients, leg pain was found to be due to foraminal encroachment upon the first sacral nerve from collapse of the disk space. Forty-one patients developed solid bony fusions and one had failure of fusion. The failure occurred in the oldest patient operated on, a woman aged 57 years.

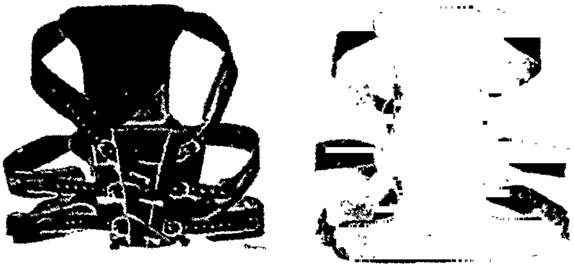

Fig. 7.—Goldthwait back brace.

The fusions have been done according to a modified Hibbs technique. Partial denervation of the joint is accomplished by total excision of the ligamenta flava. In addition, the cartilage, synovia, and capsular membranes of the facet joints have been removed. The defect in the facet is filled with bone chips from the adjacent lamina. The laminal arches of the fifth lumbar and first sacral vertebrae have been subjected to erasion, and the fusions have been completed with cancellous bone taken from the posterior superior spine of the ilium. Partial interruption of the nerve supply to the lumbosacral joint,[10] as well as decompression of the first sacral nerve roots, accounts for the improvement which patients note even in the immediate postoperative period.

No support other than adhesive tape and wound dressings has been used during the first 10 days after surgery. Between the 10th and 14th day a Goldthwait brace is fitted, which the patient wears in bed for increasing periods of time. On the 21st day ambulation is begun. The brace is worn night and day for four months and for an additional two months in the daytime only. The integrity of all fusions was tested by bending films taken nine months to one year after operation.

Results

The results in this small series of fusions are as follows: In 18 patients the results are considered excellent. The patients have no symptoms whatsoever and on physical examination demonstrate no limitation of motion in the lumbar region of the spine. Each admits to complete relief of preoperative complaints. Seventeen have had good results. Their symptoms have been relieved except for occasional mild back or leg ache, usually after exertion. However, they all demonstrate 25% loss of motion in the lumbar region of the spine, particularly in extension and lateral flexion. Two patients have had fair results, for, though fusion occurred, they complain of intermittent back and leg ache. However, both admit to considerable benefit from operation. Two are considered to have poor results. Their lumbosacral joints have fused, but they have many subjective complaints which are not explained by objective findings. One patient has a failure of fusion but is asymptomatic. Two patients have developed degenerative disk disease above the site of fusion. A woman, now aged 52, has a symptomatic lesion at the third lumbar interspace 20 years after surgery. Another woman, now aged 38, has roentgen evidence of an early degenerative lesion at the fourth space which became symptomatic after a severe respiratory infection complicated by paroxysmal coughing. Both of these complications, if they may be so termed, have been treated conservatively with relief of pain to date.

Fusion of the lumbosacral joint has proved to be an excellent procedure, for it has relieved the acute and chronic symptoms of lumbosacral arthritis in 83% of these patients. The operation provides no assurance against further episodes of back ache, for 131 movable joints remain above the area of fusion.

These patients have not all been followed for 20 years. No prophecy is made as to their future complaints. However, taken as a group, their response to operation has been most gratifying, and these operative results are far better than those in patients subjected to so-called disk surgery alone.

Summary and Conclusions

Lumbosacral arthritis is a chronic progressive disease which may be hereditary. Symptoms can appear as early as the second decade of life, but most patients develop backache from this cause in the third or fourth decades. Onset of symptoms may be acute or chronic. While severe attacks occur generally from a simple body motion, they are preceded by fatigue, emotional strain, infection, and occasionally trauma. Although backache is a constant symptom, sciatic pain may or may not be present. There is no definite correlation between collapse of the disk space and irritation of the first sacral nerve root. With progressive loss of disk space and concurrent degeneration of the facet joints, chronic symptoms appear. These may place severe limitations upon the life of the patient and can at times become incapacitating. While conservative treatment of lumbosacral arthritis is often both practical and advisable, spinal fusion in the carefully selected patient relieves the acute and chronic symptoms of the disease.

The author of an essay on backache is likely to find himself making a series of positive statements. There is harm in being always positive, for one may not be always right. The conclusions reached in this paper have not been arrived at hastily. They have been formulated after careful study. The diagnostic criteria and roentgenologic interpretations are founded upon a firm belief that degenerative disease in the lumbar vertebral joints, and especially in the lumbosacral joint, is the major cause of chronic recurrent severe low back pain with or without sciatic radiation. The treatment which has been described, while not the only approach, is reasonable, conservative, and effective.

Morbidity from low back pain is of concern to the general practitioner as well as to the specialist. There is need throughout the profession of medicine for dissemination of knowledge concerning the pathological anatomy of the spine so that the diagnosis and treatment of one of man's most common afflictions will rest upon a firmer scientific basis.

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LATE RESULTS IN OSTEOCHONDROSIS OF CAPITAL EPIPHYSIS OF FEMUR (LEGG-CALVÉ-PERTHES DISEASE)

Warren G. Stamp, M.D., Gregorio Canales, M.D.
and
Richard T. Odell, M.D., St. Louis

In treating osteochondrosis of the capital epiphysis of the femur, it has been difficult to evaluate results and consequently difficult to compare the effectiveness of various methods. There is a need for more reliable measures of hip function and better criteria of results. Of 132 patients in the present series, 34 were treated with bed rest and traction, 31 with crutch and sling, and 25 with crutch and lift; 42 received inadequate treatment or none at all. The percentage of results classified as satisfactory or fair was highest (93%) in the group with bed rest and traction. This group included 10 of the 14 patients with both hips affected. The group inadequately treated had satisfactory or fair results in only 30% of cases. Treatment by means other than bed rest and traction is feasible only if the disease is unilateral and the patient cooperates.

The management of osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease) has been controversial since the original description in 1910.[1] In 1934 Danforth[2] demonstrated the rationale of non-weight-bearing treatment to prevent deformity in the disease. In 1936 Eyre-Brook[3] compared his results of bed rest and traction versus other non-weight-bearing methods of treatment. In 1940 Gill[4] confirmed Eyre-Brook's report, and both claimed essentially normal hips as a result in every case, if therapy with bed rest and traction was begun prior to deformity. In 1951 Pedersen and McCarroll[5] reported the experience at the St. Louis Unit of Shriners Hospital for Crippled Children with bed rest and traction versus ambulatory non-weight-bearing means, and they also concluded that bed rest gave vastly improved results.

Methods

For approximately five years after Pedersen and McCarroll's report, we continued with the bed rest and traction regimen. The crutch and sling replaced the previously used crutch and shoe lift in patients whom we felt would cooperate. Since 1956, only an occasional patient has been admitted to the hospital for a full course of bed rest and traction. At present, traction is used only for a short period to allow the muscle spasm to subside, and then the crutch and sling is recommended. The patients with bilateral cases are still treated by bed rest whether at home or in the hospital. The patients in this series have all been seen at the St. Louis Unit of the Shriners Hospital for Crippled Children. When it was not possible for the patients under study to return to St. Louis for the follow-up examination, we utilized a Shriners hospital in the immediate area or an orthopedic surgeon who would complete the examination. The type of therapy recommended has not been contingent on the financial situation of the family as long as they are eligible for our service. Hospitalization is free, and we have the public school system in the hospital; thus we are not influenced for economic reasons as to which would be the ideal way of managing the patient.

We were interested in ascertaining the outcome of the original patients reported by Pedersen and McCarroll and also in determining whether it is desirable to discontinue the bed rest treatment. Mindell and Sherman[6] could not find a statistical difference between the ambulatory and the nonambulatory methods, provided the therapy was started early. Heyman and Herndon[7] used a modified program consisting of bed rest until regeneration of the femoral head was noted, 6.3 months on the average, and then followed with a non-weight-bearing brace. They reduced the hospital time without endangering the outcome of the patient.

We have seen 224 patients with osteochondrosis of the capital epiphysis of the femur between 1926 and 1957. The follow-up period has ranged from 5 to 32 years and includes 138 patients. An additional 33 patients have not completed the course of their disease and thus cannot be included in this study.

Evaluation of our results was difficult, and a sincere attempt was made to utilize the comprehensive quotient advocated by Heyman and Herndon. We found that no two observers could measure the adult deformed hip and obtain comparable figures. This difficulty arises when the epiphysis is closed, when the head is slightly or moderately deformed,

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and when x-rays are not taken with the hips in similar rotations. We used the epiphysial quotient (fig. 1) as a numerical index in evaluating our cases, and, to reduce the error of variation in measurement, one man did all the calculation. The measurement is taken as the height of the epiphysis divided by the greatest width of the head, as described by Eyre-Brook. Herndon used the width of the epiphysis, but this is not possible to measure in the patients with older cases when the line is closed and the head is deformed. The measurement for the normal hip is then divided into that for the diseased hip to determine the apparent percentage of normal. We used 40.7 as the epiphysial index in patients under 15 years old and 37.8 for patients over 15 in determining the epiphysial quotient in the bilateral cases.

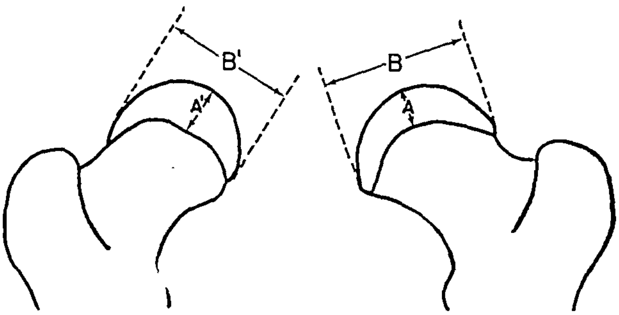

Fig. 1.—Epiphysial quotient described by Herndon but measured by Eyre-Brook's method. *Left,* normal hip. A′=21 mm.; B′=54 mm.; and index 100 A′/B′=39. *Right,* hip affected by osteochondrosis of capital epiphysis of femur (Legg-Calvé-Perthes disease). A=17 mm.; B=61 mm.; and index 100 A/B=28. Epiphysial quotient=28/29=72%.

Mindell and Sherman utilized a simple and broad classification embracing the clinical and radiographic examinations in a follow-up study of the disease. We have attempted to follow their criteria, and even with this relatively flexible classification some difficulty was encountered. A satisfactory hip (fig. 2) is one that is symptom-free but may have a few degrees of limitation of motion. The x-ray shows the hips to be without deformity. A fair result (fig. 3) has occurred when there are minor complaints, and 1 to 2 cm. of shortening will be noted. X-rays show a moderately flattened and widened femoral head, with or without acetabular changes. Patients with poor results (fig. 4) will have more pain, limp, and have some disability. There will be significant limitation of rotation and abduction. X-rays demonstrated gross deformity of the femoral head and neck and occasionally of the acetabulum.

Results in 132 Patients with Osteochondrosis of the Capital Epiphysis of the Femur (Legg-Calvé-Perthes Disease)

Method of Treatment	Patients, No.	Hips, No.	Results, No. Satisfactory	Fair	Poor	% of Satisfactory or Fair Results
Bed rest and traction	34	44	31	10	3	93
Crutch and sling	31	31	14	7	10	67
Crutch and lift	25	27	5	11	11	59
Inadequate or none	42	44	6	8	30	30

Results

The 132 patients in our series, with 146 affected hips, have been divided into four groups, according to method of treatment. The results of treatment are shown in the table. The first group was treated with traction, the second with crutch and sling, and the third with crutch and lift. The fourth group is made up of those patients who received no treatment or inadequate treatment or who were seen so late that treatment could not be expected to reverse the severe deformities already established. Those who were seen early but did not cooperate were retained in one of the three specific treatment groups, as lack of cooperation represents one of the hazards of treatment. Even after reviewing this series of cases, we are still uncertain as to the best method of treatment for patients who are seen late in the course of their disease and with seemingly severe established deformity.

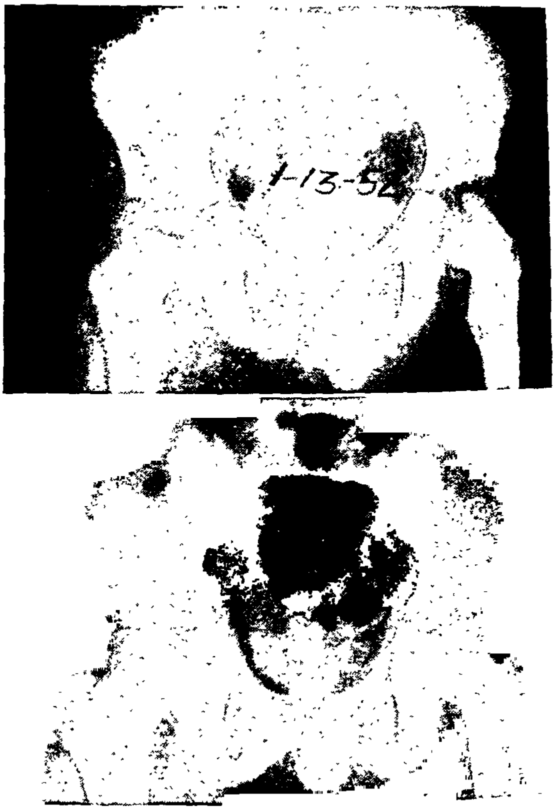

Fig. 2.—*Above,* roentgenogram made when patient was first seen at age 4. *Below,* satisfactory result, with no pain or limp, about six years later.

We attempted to correlate these results with the epiphysial quotient and found that in the groups with satisfactory results the hip was 70% or more of normal, the hips in which results were fair varied between 55% and 70%, and those in which results were poor were under 55% of normal. It was also noted that for 28% of the satisfactory hips the epiphysial quotient was lower than 70%, such as in the example shown in figure 5, which we considered satisfactory but in which the epiphysial quotient was 63. We also found that 25% of the fair results did not fall within the prescribed range and 10% of the poor exceeded 55% of normal.

All of the above patients were followed for at least 5 years and some for as long as 32 years (fig. 6). The average length of follow-up by groups is bed rest and traction, 8 years; crutch and sling, 6.6 years; crutch and lift, 12.2 years; and inadequate treatment, 19.8 years. The average follow-up period for the entire group was 11.8 years. Ninety-five per cent of the patients in this series have been seen during the six months prior to the time of writing for clinical and roentgenographic examination.

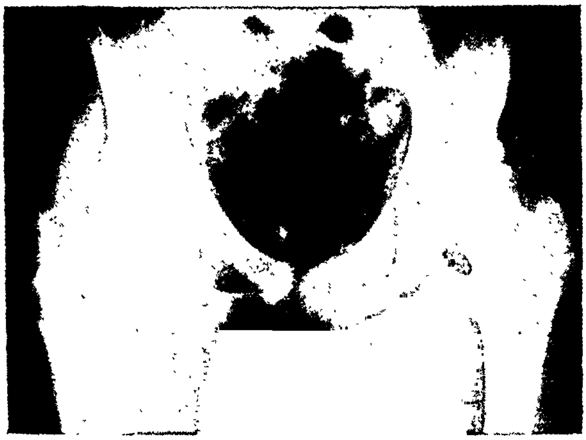

Fig. 3.—Patient treated with crutch and sling for 29 months. Fair results seven years later include no pain, no limp, negative results from Trendelenburg test, 1-in. thigh atrophy, and 0.5 in. shortening.

It is interesting that in the three so-called adequately treated groups, the length of treatment was virtually the same. In the bed rest and traction group, the average length of time this therapy was used was 17.7 months. Unrestricted weight-bearing was not permitted, however, for an additional 11.2 months, for a total treatment time of 28.9 months. Those with the crutch and sling were treated for an average of 27.4 months and those with a crutch and lift for 26.7 months. The additional therapy in the bed rest and traction group was with the use of a crutch and sling. Ten patients in the traction group were allowed unrestricted weight-bearing after traction was discontinued.

We have attempted to analyze the three poor results in two patients in the traction group. One of these two patients had bilateral involvement and was kept in bed for 56 months (fig. 7). Although therapy was begun early in this case, we still are unable to understand why it failed. The other failure was due to our error in permitting too early weight-bearing and demonstrates that even if the hip has started to regenerate flattening can occur.

Six of the 11 patients with poor results in the crutch and lift group were uncooperative, as were 6 of the 10 in the crutch and sling group. Thus, if we were to remove the uncooperative patients from these latter two groups, the number of those classified as having poor results would be virtually the same in the treated patients.

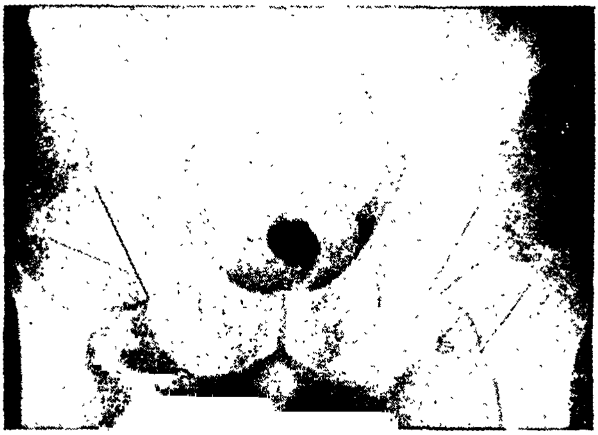

Fig. 4.—Poor result, after 31 years, in patient, first seen at age 9, with symptoms for two years. He was not adequately followed but supposedly wore an ischiatic weight-bearing brace for eight years.

Perhaps the main advantage of the traction treatment is that we force the patient to cooperate, and the calculated risk one takes in treating this disease with the ambulatory non-weight-bearing method is removed. Thirty per cent of the inadequately treated group had a satisfactory or fair result. These were not followed as closely, but 40%

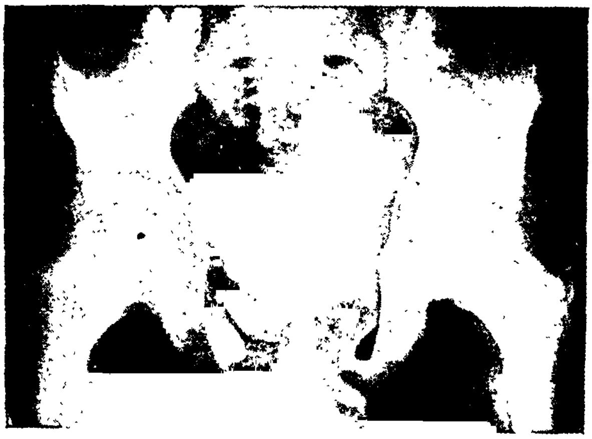

Fig. 5.—Patient, followed for eight years, with 0.5 in. shortening but no pain and no limp. Result is classed as satisfactory despite epiphysial quotient of 63. Head obviously is flatter than opposite side but if viewed alone would probably be regarded as normal.

of them may have had sufficient treatment during the vital period to at least slow down their activity and thus achieve a satisfactory or fair result many years later. This 30% did not develop the severe metaphysial changes and appeared to pass through the degenerative and regenerative phases much faster than the average. We cannot state the optimum time for full unprotected weight-bearing, but we agree with Herndon that once regeneration is started increased flattening rarely develops. We prefer to see regeneration of the outline of the femoral head before unrestricted weight-bearing is allowed in the early regenerative phase, lest too early weight-bearing lead to increased flattening of the femoral head.

It is evident from our results that treatment by bed rest and traction will insure the best results in the treatment of this disorder. It is also our contention that a patient with unilateral involvement, who can be followed closely, may be treated with a crutch and sling. Weight-bearing on the degenerating femoral head must be reduced to a minimum to get a satisfactory result. In spite of the fact that bed rest and traction have given a more uniformly satisfactory result in the treatment of this disease, we continue to use the crutch and sling. This seeming paradox arises because there are gradations in severity of this disease and when properly managed the crutch and sling method can insure satisfactory results.

Conclusions

Bed rest and traction (nonambulatory and non-weight-bearing) will insure the best results in the majority of patients with osteochondrosis of the capital epiphysis of the femur (Legg-Calvé-Perthes disease). Therapy with crutch and sling is indicated in cases of unilateral disease where instruction can be given as to the importance of non-weight-bearing methods. Inadequate treatment carries a 70% chance of causing a poor result. Ambulatory non-weight-bearing methods must be replaced with bed rest if the patient is unable to cooperate.

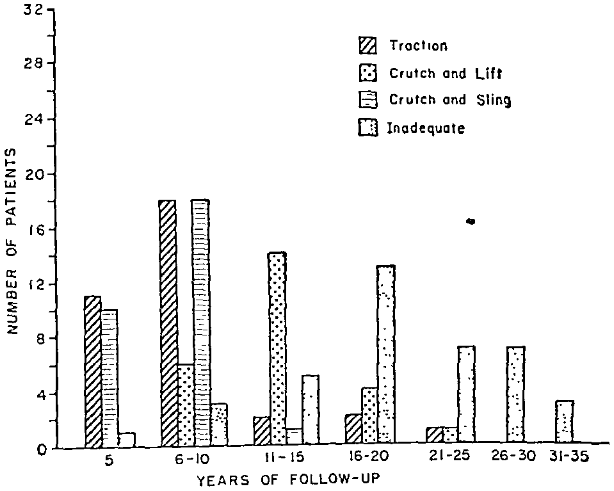

Fig. 6.—Length of follow-up in 132 patients.

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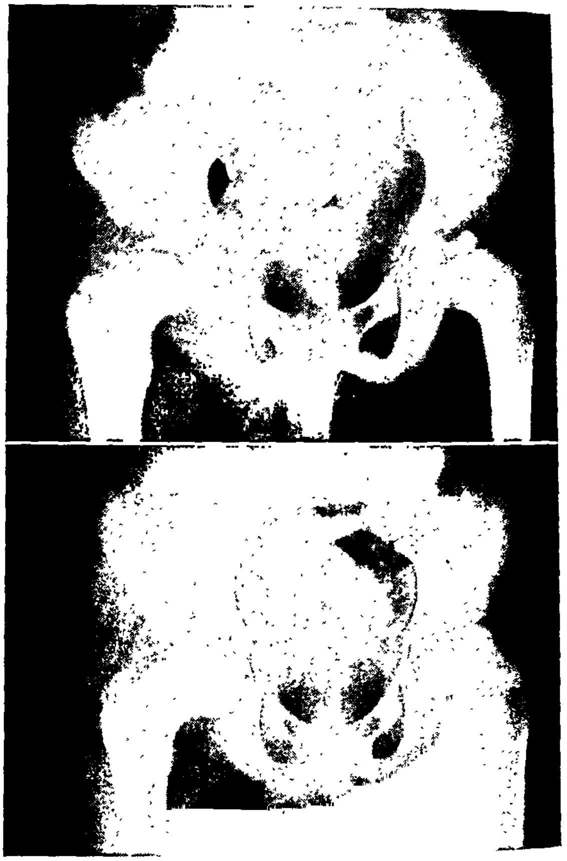

Fig. 7.—*Above,* 4½-year-old boy with pain in left hip and knee for 12 months; no treatment prior to our examination. Patient was started on bed rest and traction. *Below,* marked limitation of rotation, no pain, cystic area remaining in left femoral head. Result is presently classified as poor but may improve to fair. Epiphysial quotient is 55 on right and 45 on left.

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PATHOLOGY OF JAUNDICE RESULTING FROM INTRAHEPATIC CHOLESTASIS

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Organic disease of the liver can cause cholestasis by mechanical hindrance at any level from the bifurcation of the common hepatic duct to the septal bile ducts within the small portal tracts; moreover, protracted cholestasis from any cause provokes enough inflammatory exudation and connective tissue formation to add a secondary intrahepatic mechanical obstructive component. The more difficult problems in differential diagnosis are presented by cases in which cholestasis occurs without tangible mechanical explanation. Certain drugs, endocrinopathies, and viral infections must then be considered as possible causes. The biliary concrements found in children with the "inspissated bile syndrome" are probably the result rather than the cause of obstructive phenomena. Liver biopsy is sometimes helpful in diagnosis, but at times surgical exploration or percutaneous cholangiography becomes necessary.

Jaundice with impairment of bile flow is said to result either from a disturbance at the site of bile formation, the epithelial cells of the liver, or from interference with the flow in the biliary passages without necessarily being associated with alteration of the liver cells. The mechanism of an obstruction to the bile flow in the extrahepatic bile ducts, for instance, by stones, tumors, or strictures, or jaundice from liver cell injury, appears obvious, and the pathological causes are established. In contrast, interference with the bile flow within the intrahepatic biliary passages is still shrouded in mystery. Although little agreement exists as to both the pathological causes and the mechanism, it might be profitable to review once more the thorny problem which has puzzled clinicians and pathologists since Naunyn's and Hanot's time and which represents one of the main difficulties in the differential diagnosis between "medical" and "surgical" jaundice. It has become more pressing in recent years because therapy with various drugs has produced this type of jaundice with increasing frequency.

Nomenclature

Interference with bile flow in the biliary passages in the liver, as clinically reflected in jaundice with pruritus, and functionally, in elevation of serum alkaline phosphatase activity, and often in total serum cholesterol activity, has been designated by various names. "Intrahepatic biliary obstruction"[1] implies a mechanical obstacle which frequently is not demonstrable. "Cholangiolitis"[2] presupposes an inflammatory process not necessarily present and usually assumed to be in the "cholangioles" by exclusion rather than by actual demonstration. "Periacinose hepatitis"[3] implies a specific localization not found in all cases. It therefore may be advantageous to use the noncommittal term "intrahepatic cholestasis"[4] until the phenomenon is better clarified. Intrahepatic cholestasis, defined functionally rather than structurally, may be the only abnormality present or the predominant one, or it may be just a component of a hepatic disease associated with damage of the liver cells with its functional characteristics.

For any attempt of localization, agreement upon the designation of the anatomic structures is required (fig. 1). The initial biliary radicles lined by the hepatic cell walls thrown into fine microvilli seen under the electron microscope are best designated as bile canaliculi or bile capillaries. They form a chicken-wire-like network separated under normal circumstances from the blood capillaries by half the width of the hepatic cell.[5] They are connected with the bile ducts in the portal tracts by narrow tubes lined by cuboid epithelium with similar microvilli. These tubes, mainly located around the portal tract and far less frequently within the lobule, are best called ductules, although the terms canal of Hering, ampulla, and intermediate pieces (Zwischenstücke) have been applied. The term "cholangioles" creates confusion, since some use it to designate bile canaliculi and others ductules or even the small septal bile ducts.

Intrahepatic Biliary Obstruction

Intrahepatic cholestasis may be produced by mechanical obstruction demonstrable by morphologic means, or it may be apparent only from its

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consequences, i. e., bile imbibition without obvious structural causes. Bile pigment is found predominantly in the lobular center in the hepatic cells, usually staining protein coagulums varying in size, in bile plugs in the bile canaliculi, and diffusely staining the cytoplasm of the Kupffer cells. In prolonged jaundice, secondary liver cell injury is indicated by a *rarefication of the cytoplasm* (*feathery degeneration*) followed by loss of cells and accumulation of scavenger cells. Bile also accumulates on the lobular periphery, and sometimes proliferated ductules contain microcalculi (fig. 2).

Mechanical obstruction may be located in the larger intrahepatic bile ducts, in the small septal bile ducts within the portal tracts, or in the ductules.

Obstruction at Bifurcation of Common Hepatic Duct.—Occlusion at the forking of the common hepatic duct involves the most proximal point of the main axis of the total bile flow and thus regularly produces jaundice just as lesions of the extrahepatic biliary ducts. Although the process is actually intrahepatic, its clinical and functional manifestations are those of an extrahepatic lesion.

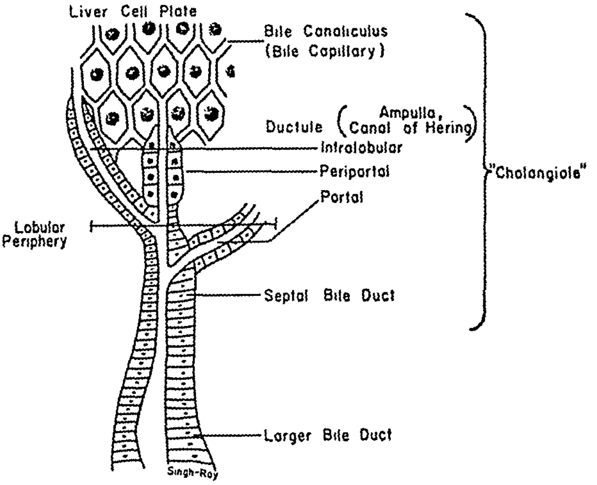

Fig. 1.—Illustration of nomenclature of intrahepatic biliary passages.

Obstruction of Larger Intrahepatic Bile Ducts.—Compromise of the lumen of one main branch of the common hepatic duct without involvement of the other, for instance, by carcinoma, by stone, or after operation, produces elevation of the serum alkaline phosphatase level but no, or only transient, jaundice because the unobstructed part of the biliary system excretes the retained bile in a compensatory fashion. Rarely is obstruction of intrahepatic bile ducts outside of the smallest portal tracts widespread enough to produce persisting jaundice. Diffuse carcinomatosis of the liver and considerable parenchymal damage complicating local obstruction are exceptions. In very rare instances, xanthomatous areas around the intrahepatic bile ducts also produce cholestasis (fibroxanthomatous cirrhosis).[6] However, space-occupying lesions may produce focal bile stasis. Thus, morphologic evidence of bile stasis in liver biopsy specimens in the absence of jaundice suggests such a lesion, particularly metastatic carcinoma.

Obstruction of Septal Bile Ducts Within the Small Portal Tracts.—In a variety of conditions, the bile flow in septal bile ducts and ductules in the portal tract may be interfered with by compression, disruption of their continuity, or alteration. The evidence that accumulation of inflammatory exudate compresses the ductules is not convincing, since large amounts of exudate may accumulate without jaundice. Leukemic infiltration of portal tracts, even if severe, is not accompanied by jaundice. Similarly, severe portal fibrosis with portal hypertension, as in schistosomiasis, or granulomas, such as in sarcoidosis, does not necessarily produce jaundice. The only reliable morphologic evidence of a biliary obstruction within the portal tract is the absence of septal bile ducts or ductules within the inflamed or scarred portal tract. This occurs on a developmental basis in the rare instances of intrahepatic ductal atresia called acholangic biliary cirrhosis.[6] Of greater importance is the disappearance of ductules and ducts which has been considered the anatomic basis of the protracted jaundice occurring mainly in older women and frequently associated with hypercholesteremia and xanthomatosis. This lesion, as the most important representative of the syndrome of primary biliary cirrhosis (see below), has been designated as pericholangiolitic biliary cirrhosis [6] (fig. 3*A*). If the ductules are present, their morphologic alterations, namely, excessive proliferation, distortion, and fibrosis around them, are not as clearly established as causes of mechanical intrahepatic obstruction because similar features can apparently be found without jaundice. Such entities as obliterating cholangitis [7] and subacute cholangiolitic biliary cirrhosis [8] belong to this group. The French author Albot [9] lists two other entities: (1) *obstructive cholangiolitis* in the course of Rössle's nonobliterating diffuse cholangitis and (2) diffuse mesenchymatous hepatitis with nodular lymphomatosis of Hanot and Kiener. Further anatomic studies should identify the morphologic appearance of ductular alterations which exert an obstructing effect. Disruption of the ductules seems also to account for relatively acute jaundice in Hodgkin's disease.

Periportal Ductular Destruction.—In prolonged cholestasis of both intrahepatic and extrahepatic types, bile imbibition of the hepatic cells on the lobular periphery is associated with degenerative changes of these cells reflected also in the presence of granules giving a periodic acid Schiff reaction even after diastase treatment. This is accompanied by some inflammatory exudation and the appearance of collagenous fibers around these cells and their neighboring ductules, all of which disintegrate. The fibers seem to aggregate, forming a continuous collagenous barrier between these liver cell plates and their draining ductules (fig. 3*B*). Therefore, in both intrahepatic and extrahepatic protracted cholestasis from any cause, a secondary intrahepatic mechanical obstructive component is added. It may account for persisting jaundice after surgical correction of a protracted extrahepatic obstruction.

The end stage of all the lesions listed is biliary cirrhosis, designated as primary biliary cirrhosis[10] if the extrahepatic biliary tract is not involved. The connective tissue may aggregate in the portal spaces or abound within the parenchyma (hypertrophic cirrhosis of Hanot). In the earlier stages, the altered reconstruction of the lobular parenchyma reflected in regenerative nodules and formation of septums connecting portal tracts and central canals is still in the background, and the manifestations of cholestasis dominate the picture. In advanced stages, all signs and symptoms of cirrhosis are present.

Intrahepatic Cholestasis Without Structurally Demonstrable Causes

Conditions falling under the heading of intrahepatic cholestasis without structurally demonstrable causes are of particular differential diagnostic importance, and far more frequent clinical examples are seen than in the group with obvious obstruction. However, the lack of an established pathogenesis permits only an enumeration of examples rather than a rational classification.

Intrahepatic Cholestatic Component of Hepatic Disease.—In almost all hepatic diseases associated with diffuse liver cell injury, the degree of jaundice may not be directly related to the degree of hepatocellular damage or that of hemolysis. In such instances it is well correlated with the degree of cholestasis as morphologically seen in the liver and with the results of hepatic tests assumed to reflect cholestasis. These are increases of serum alkaline phosphatase activity and total serum cholesterol and reduction of fecal and urinary urobilinogen. On this evidence rests the assumption that an intrahepatic cholestatic component accounts at least for part of the jaundice in various types of hepatitis and cirrhosis.[11] Between the two extremes of liver cell injury without cholestasis and cholestasis without liver cell injury, all degrees of combinations may occur in different patients and in different stages of the same disease in an individual patient.

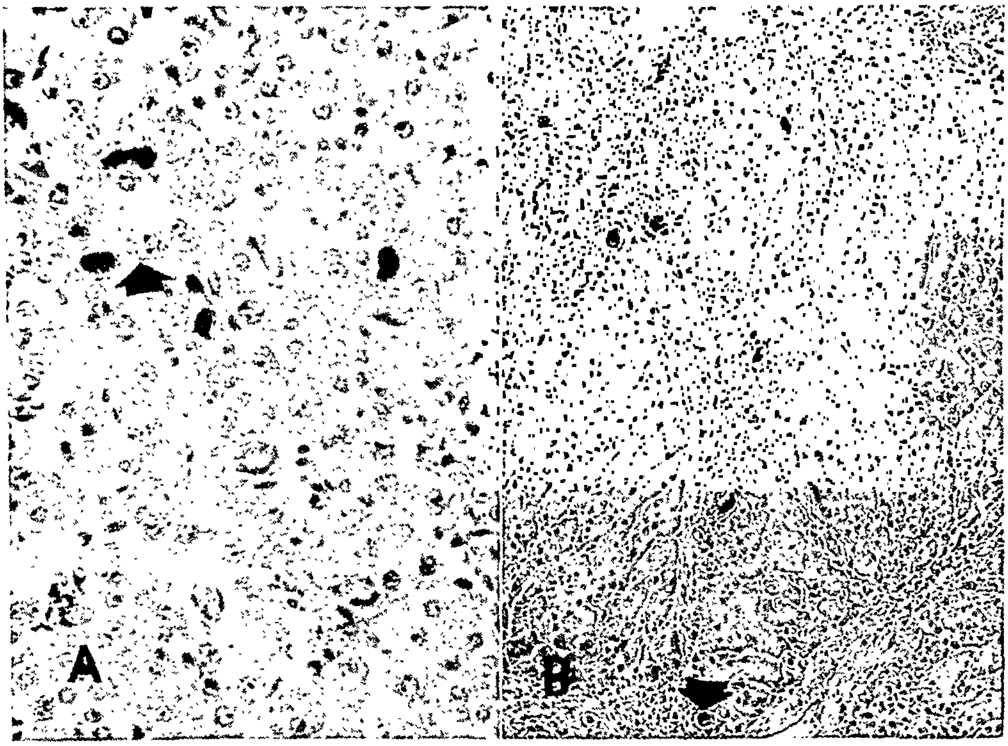

Fig. 2.—*A*, bile stasis in center of lobule reflected by presence of bile in form of various sized granules in liver cells (*arrow*), in casts in bile canaliculi, and in Kupffer cells. Hematoxylin and eosin stain (× 240). *B*, intrahepatic bile stasis in postnecrotic cirrhosis evidenced by microcalculi in proliferated ductules and in septal bile duct (*arrow*). Hemotoxylin and eosin stain (× 63).

The question of surgery because of assumed extrahepatic biliary obstruction may arise, but here liver biopsy is helpful in clarifying the nature of the disease process. In rare cases of viral hepatitis with an otherwise typical morphologic picture, cholestasis is clinically in the foreground.[12] More frequently, cholestasis predominates in one phase of an otherwise clinically typical instance of viral hepatitis.[4] Cholestatic features may also complicate large fatty livers with jaundice, diffuse septal cirrhosis, and particularly active stages of postnecrotic cirrhosis in which the deposition of microcalculi in ductules may be conspicuous. A cholestatic component may also be in the foreground of various hepatic disorders of vague etiology, such as "toxic hepatitis" occurring after operation or in the neonatal period.

Intrahepatic Cholestasis as Dominant Feature of Hepatic Disease.—Probably the most difficult differential diagnostic problems are presented by a group of cases in which cholestasis without a tangible anatomic substrate is clinically, functionally, and structurally in the foreground. Liver cell damage, if present, is relatively mild or is frequently the result of the cholestasis if feathery degeneration of liver cells is seen. In the early stages, inflammatory reactions in the parenchyma and in the portal tracts may be absent. They are regularly present after several weeks' duration and the term cholangiolitis then appears appropriate.[11] They probably are the result of the lesion rather than its cause.

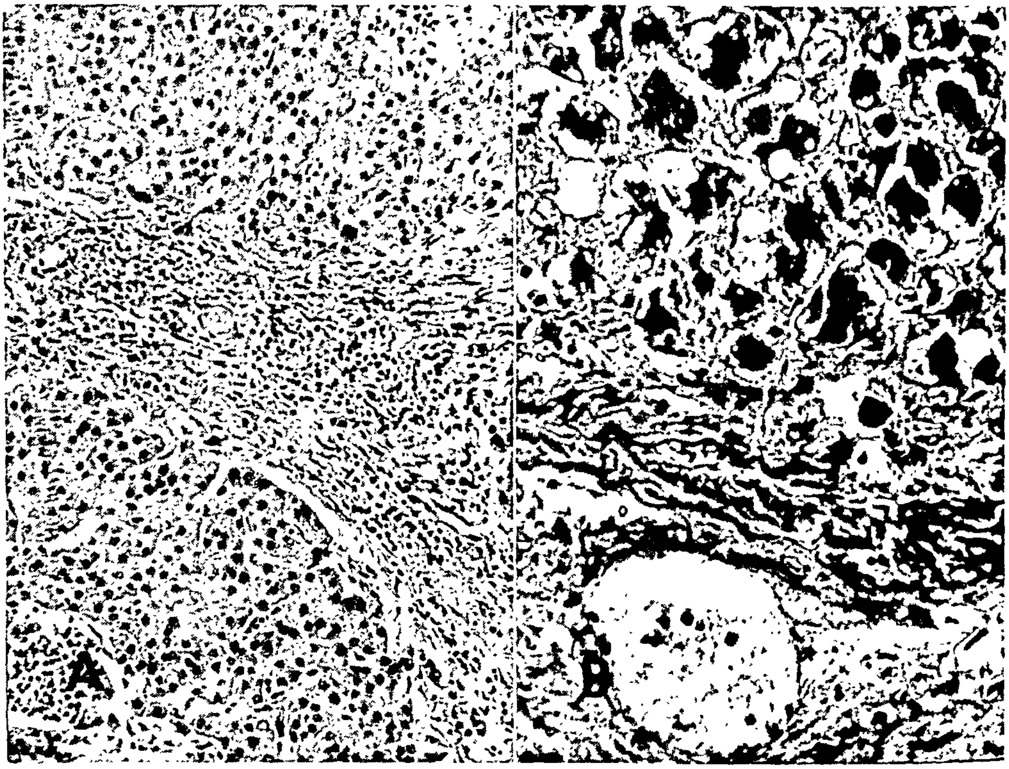

Fig. 3.—*A*, absence of bile ducts and ductules in trabeculae of pericholangiolitic biliary cirrhosis with xanthomatosis. Hematoxylin and eosin stain (× 120). *B*, aggregation of collagenous fibers on border between portal tract and parenchyma containing degenerating liver cells in secondary biliary cirrhosis after stricture of common bile duct. Mallory aniline blue stain (× 240).

In chronic stages the picture of pericholangiolitic biliary cirrhosis previously referred to may appear. However, the incidence of the progression of the cases of this group into primary biliary cirrhosis still remains to be established. In view of the absence of characteristic inflammatory changes, liver biopsy may not be of great assistance in the separation from extrahepatic biliary obstruction. It may become more helpful but also more dangerous after several weeks. Then extrahepatic biliary obstruction may have produced diffuse dilatation of the entire biliary tree. This mechanical pressure effect of hydrohepatosis is histologically reflected in the pathognomonic findings of bile infarcts and bile extravasation. Drugs of quite divergent nature chemically are reported, in increasing numbers, to produce cholestasis. In another group of cases, at present better designated as idiopathic, the etiology is unknown or at best doubtful.

Drug-Induced Intrahepatic Cholestasis: Of the various drugs producing intrahepatic cholestasis associated with little or no liver cell injury, chlorpromazine (Thorazine) seems to be the most important in recent years from the point of view of incidence.[13] In cases of intrahepatic cholestasis produced by arsphenamine,[1] chlorpromazine, para-aminosalicylic acid,[14] thiouracil, and sulfanilamide, portal infiltration has been present. In cases produced by methyltestosterone,[15] norethandrolone (Nilevar),[16] para-aminobenzoyl caffein hydrochloride, methimazole (Tapazole), and sulfadiazine, portal infiltration has not been present. Although all of the drugs produce the same structural and functional manifestations of cholestasis, only some elicit at least temporary inflammatory reactions in the portal tracts reflected in accumulation of lymphocytes, histiocytes, and segmented leukocytes, many of which are eosinophilic, associated with proliferation of ductules and circulating eosinophilia (fig. 4*A*). This lesion has been called allergic cholangiolitis [4] and has been implicated in the development of the cholestasis.

However, this portal reaction is absent, for instance, in jaundice produced by methyltestosterone [15] or norethandrolone [16] (fig. 4*B*). It may be present without jaundice in reactions produced by chlorpromazine or para-aminosalicylic acid.[14] Moreover, morphologically identical reactions may occur without previous drug therapy in random liver biopsy specimens [16] or in systemic hyperergic reactions without jaundice. In patients dying with progressive cholestasis from chlorpromazine treatment, the portal tract may be entirely normal even if preceding liver biopsies demonstrated portal reactions.[11] It thus appears that cholestasis and portal inflammatory reactions (hyperergic or not) are independent phenomena. In a very few patients exposed to chlorpromazine [17] or arsenicals,[18] transition into what has been called primary biliary cirrhosis with xanthomatosis has been reported.

Idiopathic Intrahepatic Cholestasis: The ill-defined group of patients with idiopathic intrahepatic cholestasis includes those with possible endocrine disturbances, particularly if jaundice develops during the menarche or menopause, and patients with suspected viral hepatitis,[2] at least on epidemiologic grounds, in which case it is an extreme of the condition discussed in the section on cholestatic component of hepatic disease.

Pathogenesis

Intrahepatic biliary obstruction as a mechanism producing cholestasis requires no further consideration. Since intrahepatic biliary obstruction develops in chronic stages of all forms of cholestasis, the pathogenesis of acute cholestasis in both the pure form and as a component of hepatic disease is the major problem. Much has been written about this since Naunyn assumed an alteration of the polarity of the bile flow from liver cells into the blood stream. Recent morphologic and biochemical investigations have pointed to the probable site of cholestasis although not to its mechanism. The morphologic integrity of the liver cells and the usually normal results of hepatic tests indicating hepatocellular damage as well as the presence of bile within the intraparenchymal biliary passages speak against impairment of hepatic cell function. The bilirubin in the serum gives a direct van den Bergh reaction and, therefore, interference with its glucuronide conjugation is unlikely.

Since no evidence exists for any anatomic alteration of the septal or larger bile ducts, cholestasis had been localized in the bile canaliculi or ductules (fig. 5). The possibility that an actual obstruction

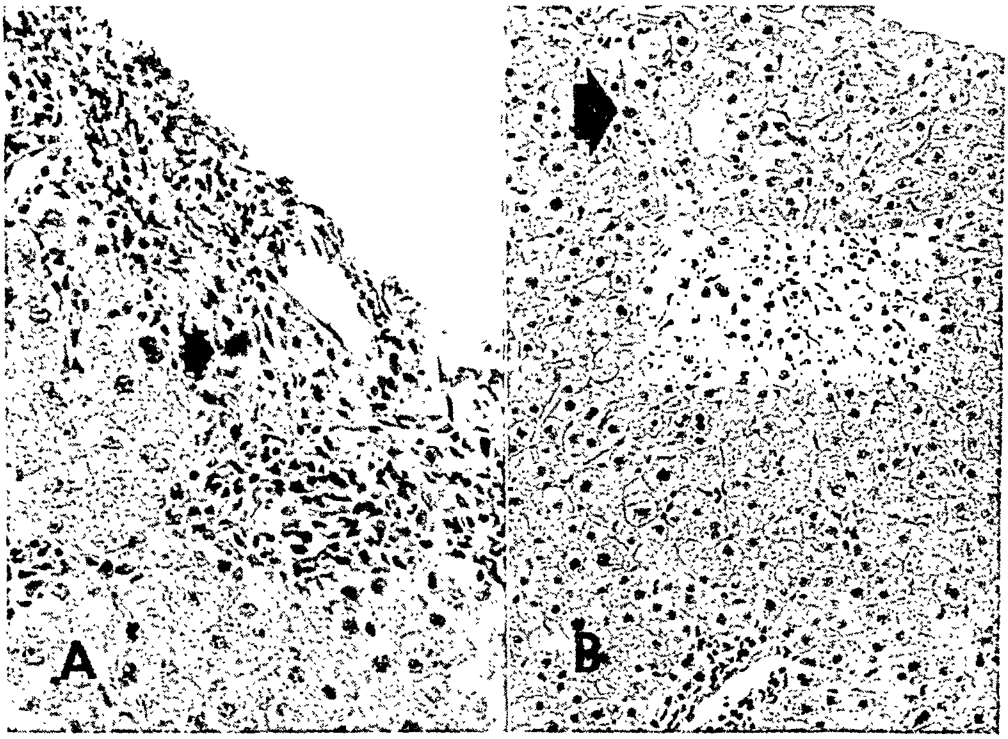

Fig. 4.—*A*, accumulation of segmented leukocytes, including many eosinophils, histiocytes, and lymphocytes and proliferation of ductules (*arrow*) in edematous small portal tract indistinctly delineated from surrounding parenchyma in liver biopsy specimen from patient with jaundice occurring after administration of chlorpromazine. Hematoxylin and eosin stain (× 240). *B*, intrahepatic cholestasis in centrolobular zone (*arrow*) in absence of alterations of portal tract in biopsy specimen from patient who had received norethandrolone. Hematoxylin and eosin stain (× 120).

exists within the bile canaliculi or ductules by either swollen, disorganized, or regenerating liver cells, or by bile plugs in the canaliculi or ductules, is negated by the presence of bile, at least in some cases, along the entire length of the bile canaliculi and ductules. Occasionally bile may even be seen under these circumstances in the form of microcalculi in the septal bile ducts. These findings suggest that the bile is inspissated or altered in its constitution. This is supported by the frequent occurrence of biliary concrements in the extrahepatic biliary ducts which gave rise to the term "inspissated bile syndrome" in children. They are more probably a reflection of altered bile rather than the cause of obstruction, especially since the biliary passages are not dilated.

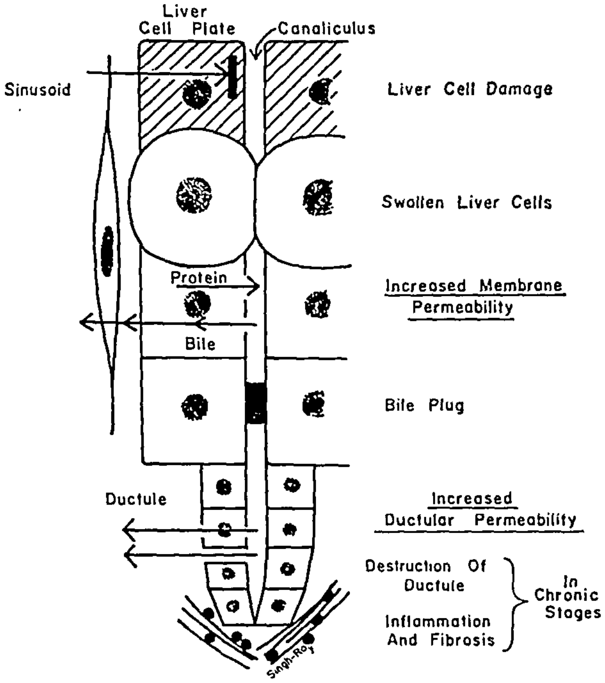

Fig. 5.—Illustration of possible mechanisms responsible for intrahepatic cholestasis.

Inflammation around the ductules and ducts in the portal tract (cholangiolitis) has already been excluded as a pathogenetic factor since it is not always present in cholestasis and may be present in the absence of jaundice. Thus, a permeability change, as previously assumed,[2] appears to account for intrahepatic cholestasis. Permeability may be increased in two opposite directions. Regurgitation of biliary substances from canaliculi or ductules may account for jaundice and possibly also for periductular inflammatory reactions. Moreover, a relatively greater backflow of fluid rather than solids may explain the dehydration and inspissation of bile with formation of bile plugs. Increased permeability in the other direction with oozing of protein from the liver cells into the bile (albuminocholia) [3] may increase the viscosity of the bile, leading to its inspissation. Material, apparently carbohydrate-protein complexes, is stained with the periodic acid Schiff reaction around bile plugs.

The alteration of the bile by possibly both dehydration and albuminocholia may best explain acute intrahepatic cholestasis. Differences in the conjugation of bilirubin in the bile deserve further study. The permeability alteration seems to be localized in the hepatic cell membrane lining the bile canaliculus and possibly also in the ductules. Further study of the microvilli visible under the electron microscope in these locations may clarify the time-worn problem of the pathogenesis of hepatogenous jaundice.

Conclusions

Intrahepatic cholestasis results from mechanical obstruction or has no demonstrable pathogenesis. The latter process seems to be a characteristic reaction of the liver to a variety of injuries. It may be only a component of a hepatic disease with structural and functional involvement of the liver cells and is, therefore, found in any type of cirrhosis or hepatitis. On the other hand, intrahepatic cholestasis may be an independent phenomenon which either is induced by drugs or is of unknown (idiopathic) etiology. The acute and subacute stages of nonobstructive intrahepatic cholestasis, more so than with demonstrable mechanical obstacles, present a difficult differential diagnostic problem because of similarity to the "surgical" type of jaundice in extrahepatic biliary obstruction. Clinical observations and hepatic tests may not provide the answer, while liver biopsy is helpful only in the presence of positive findings such as the "hyperergic" type of portal inflammation in drug-induced cholestasis or the effects of hydrohepatosis in mechanical obstruction. Surgical exploration or percutaneous cholangiography may still be a diagnostic last resort.

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CLINICAL ASPECTS OF JAUNDICE RESULTING FROM INTRAHEPATIC OBSTRUCTION

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The various disorders associated with jaundice resulting from intrahepatic obstruction represent a major clinical problem in adult patients with icterus. Fundamentally all instances of jaundice not caused by a gross mechanical obstruction to the free outflow of bile from the liver represent intrahepatic obstruction. Popper's classification of jaundice,[1] i. e., according to impairment or nonimpairment of bile flow, is a helpful approach in discussing the mechanisms involved. In clinical practice, instances of jaundice without impairment of bile flow (jaundice associated with over-production of free bilirubin as in hemolytic disorders and retention jaundice, as in constitutional hepatic dysfunction), can usually be recognized without undue difficulty. Chronic idiopathic jaundice (Dubin-Johnson syndrome) is probably not associated with a significant quantitative reduction in total bile flow despite the mild degree of regurgitation jaundice that characterizes the condition. The diagnosis can be established by clinical study and liver biopsy. It is not customarily included in discussions of jaundice resulting from intrahepatic obstruction.

Currently drug sensitivity reactions are responsible for most instances of self-limited jaundice due to primary intrahepatic cholestasis. Icterus associated with chlorpromazine therapy represents a classic example. The development of jaundice after the drug therapy is discontinued and the occurrence of prolonged jaundice are illustrated in two patients as uncommon but noteworthy examples of this drug idiosyncrasy. In a third case, a 54-year-old man became jaundiced after four months' medication with methyl testosterone. A chronic progressive form of jaundice resulting from intrahepatic obstruction is exemplified by a 47-year-old woman with primary biliary cirrhosis of unknown etiology. The slowly increasing rise of the serum bilirubin level was temporarily reversed by steroid therapy. This effect was more likely due to the suppression of a mild concomitant hemolytic than to an effect on her liver disease. Subsequently the serum bilirubin level rose again. Death occurred after hemorrhage from esophageal varices.

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Patients with impaired bile flow exhibit regurgitation jaundice; increased amounts of both conjugated and free bilirubin are present in the blood serum. The major problems in differential diagnosis are encountered in patients with regurgitation jaundice. The term cholestasis is useful in a descriptive sense for a discussion of the phenomenon of impaired bile flow in the liver itself. Cholestasis produced by extrahepatic obstruction, i. e., "surgical jaundice" due to gallstones, cancer, or stricture, usually presents a fairly well-defined clinical, biochemical, and morphologic picture. On the basis of careful clinical studies, the existence of extrahepatic biliary obstruction can be correctly predicted preoperatively in 90% of surgical cases. The problem cases encountered in the 10% group are mainly in patients who have moderately severe hepatocellular damage associated with the obstruction or who have unusual types of obstructing lesions.

Cholestasis resulting from an intrahepatic obstruction to the flow of bile presents a more formidable problem in diagnosis. Intrahepatic cholestasis is a component in the majority of patients who exhibit hepatocellular degeneration, i. e., viral hepatitis, toxic liver injury, and the various forms of cirrhosis.[1] When the component of hepatocellular degeneration predominates, a correct diagnosis of the hepatic condition can usually be established without undue difficulty. The clinical features are fairly distinctive, and the biochemical and the morphologic changes (as seen in a biopsy specimen) are revealing. Unfortunately the component "cholestasis" is not accompanied by a specific recognizable morphologic lesion; the deposition of bile pigment in the liver cells and in the canaliculi is nonspecific. Intrahepatic cholestasis may at times be the major or predominant component of a liver disorder that ordinarily is considered to be a typical example of jaundice due to hepatocellular degeneration.

Thus the physician is occasionally confronted by a patient with viral hepatitis or cirrhosis in whom the degree and duration of icterus and other evidences of biliary obstruction seem out of proportion and unusually prominent when compared with the average or classic case. This is reflected in the clinical picture; i. e., the patient may be more jaundiced than ill. It is reflected in the biochemical picture; i. e., the bilirubin, alkaline phosphatase, and lipid pattern indicate obstruction while the quantitative and qualitative changes in the serum proteins characteristic of hepatocellular damage are often minimal. Yet, even when cholestasis is a major component in cirrhosis or in viral hepatitis, an experienced pathologist can usually recognize the basic underlying disturbance by a careful study of the liver biopsy.

Gall and Braunstein[2] emphasized that in viral hepatitis the fundamental morphologic features can be recognized in biopsy specimens, even though the pathologist may not be able to predict which patients exhibit clinical or biochemical manifestations simulating excretory impairment and which patients exhibit the accepted clinical and biochemical evidences of hepatocellular degeneration. The recognition of intrahepatic cholestasis as the predominant component of certain liver disorders associated with jaundice can often be accomplished by analyzing a combination of clinical, laboratory, and histological evidences. It must be admitted that some patients do present extremely complex problems. The variables inherent in extrahepatic biliary obstruction (cholestasis with hepatocellular damage as a variable component) and the hepatitis-cirrhosis-toxic liver injury group (hepatocellular degeneration with cholestasis as a variable component) are very great indeed. At times the correct diagnosis cannot be established until the exact status of the extrahepatic bile duct system is determined.

In certain patients cholangiography must be performed. In these complex situations the safest course is to treat the patient as a medical problem for four to six weeks before resorting to operation. The arbitrary period of study and medical treatment of these diagnostic problem cases admittedly constitutes a hardship for the patient who ultimately proves to have a surgical lesion. However, it is likely to be lifesaving for the patient with medical jaundice in whom early surgical intervention is not only unrewarding but actually hazardous.

Jaundice due to intrahepatic obstruction is not limited to patients with hepatocellular degeneration, i. e., cirrhosis, viral hepatitis, or toxic liver injury. Manifestations of cholestasis may be the sole component discernible in certain liver disorders in which the liver cells appear normal and the extrahepatic duct system is completely patent, i. e., primary intrahepatic cholestasis. The patient with jaundice due to chlorpromazine sensitivity is a classic example. A number of drugs have been incriminated in the hypersensitivity reactions that produce primary intrahepatic cholestasis. In rare instances no cause can be definitely established.

The basic mechanism involved in primary intrahepatic cholestasis is unknown. If a single mechanism is involved, it is presumed to be a regurgitation of bile back through morphologically intact "cholangioles." (The term cholangiole has been used broadly to include the biliary canaliculi, the ductules, and the terminal ducts.[3] As used in current American literature the term presumably includes the ductules—intralobular and perilobular ducts—and the interlobular ducts, but not the canaliculi.) One must assume that a functional derangement in the cholangioles permits biliary substances to leak back into the tissues and eventually to regurgitate into the lymph and blood. This explanation is invoked to account for the presence of bile thrombi in the canaliculi up to but not beyond the ductules, the apparently normal histological appearance of the ductules and ducts and the pericholangiolitis. The inflammatory reaction is presumably due to irritation produced by substances in bile.

The explanation has been offered that an increased permeability of the cholangioles favors an increased absorption of water with a resultant inspissation of bile. The occurrence of bile plugs or thrombi, so prominent in intrahepatic cholestasis, is thought to be on this basis. Bile thrombi themselves are not believed to be the fundamental cause of the intrahepatic obstruction. One must accept the fact that the morphologic evidences of cholestasis, i. e., the bile staining, the bile plugs, the inflammatory reaction, and the evidences of parenchymal cell injury (usually very minimal and insignificant in primary intrahepatic cholestasis) are probably secondary to the stasis of bile rather than its cause.

The critical student of the subject may not be entirely satisfied with the explanation that a functional impairment of the cholangioles, i. e., an increased permeability, is responsible for jaundice due to intrahepatic obstruction. This has been regarded as a plausible explanation to account for the available biochemical and histological observations. The inability to produce a liver lesion in an experimental animal that completely mimics primary intrahepatic cholestasis as seen in man is a distinct handicap in fundamental investigations of this important subject. The experimental studies of Hanzon[4] dealing with basic mechanisms involved in regurgitation jaundice did not indicate that the ductules or ducts exhibited an undue vulnerability as a site of bile escape. In graded liver cell injury and in the early stages of extrahepatic obstruction, regurgitation of bile (visualized by virtue of fluorescent uranin) was observed to occur directly from intact canaliculi and from morphologically intact liver cells.

The apparent absence of a specific morphologic lesion in primary intrahepatic cholestasis disturbs the pathologist in his attempts to explain the pathogenesis of the disorder. The absence of a specific lesion also constitutes a very real obstacle in the practical problem of establishing the diagnosis on the basis of a liver biopsy specimen. The similarity of the histological appearance of the liver irrespective of whether cholestasis is due to intrahepatic or extrahepatic obstruction has been emphasized repeatedly. At times the hydromechanical effects of extrahepatic obstruction are sufficient to produce specific morphologic changes that have diagnostic value. However, when liver biopsies are performed early, i. e., within the first two or three weeks of the onset of jaundice, the pathologist may not be able to make the distinction.

Primary intrahepatic cholestasis presents a clinical picture that may be easily confused with some forms of extrahepatic biliary obstruction, since the features are often those of icterus and pruritus without signs of toxicity or sepsis. The liver tests are not usually distinctive; the alkaline phosphatase and lipid levels are elevated in both conditions, and the abnormalities in the proteins (quantitative or qualitative) are usually minimal in each type. Fortunately, many instances of intrahepatic obstruction, especially cases of drug-induced jaundice, are self-limited and soon relent. A correct diagnosis can often be established during the course of clinical observation and medical treatment. Occasionally cases of protracted jaundice due to primary intrahepatic cholestasis are encountered, and an operative cholangiogram may be required to establish the diagnosis with absolute certainty. In selected instances this may be performed under local anesthesia through a small abdominal incision.

Acute (Self-Limited) Forms of Jaundice Resulting from Intrahepatic Obstruction

Drug reactions are responsible for the majority of instances of primary intrahepatic cholestasis that are currently encountered in clinical practice. The characteristic histopathological and biochemical features of this type of reaction were described in 1940 by Hanger and Gutman in cases of arsphenamine sensitivity, and in the ensuing 18 years[5] a number of other drugs have been incriminated as causative agents. Jaundice due to chlorpromazine has been the most common cause of this reaction in recent years.

Jaundice due to Chlorpromazine.—The incidence of jaundice due to chlorpromazine (Thorazine) hydrochloride is stated by the manufacturer to be "low," but in view of its administration to more than 10 million patients, even a low incidence of this reaction results in a large number of individuals with icterus. There have been many opportunities to study the problem; the literature has been reviewed in recent reports.[6] Although the pattern of reaction has varied somewhat, the majority of patients develop jaundice during the second or third week of the drug administration. The onset of jaundice is often preceded by three or four days of prodromal symptoms that include fever, malaise, anorexia, and indefinite gastrointestinal symptoms. At times patients experience mild degrees of abdominal pain at the onset. The jaundice is typically obstructive in type with dark urine and light stools.

With the onset of jaundice many of the symptoms disappear, and, save for pruritus, the patients become relatively comfortable. The prostration that usually attends viral hepatitis is customarily lacking in patients with jaundice due to chlorpromazine. Fortunately, the intrahepatic obstruction to bile flow usually relents within a few weeks to two months, and the patients recover uneventfully. Although most observers regard the disorder as a hypersensitivity phenomenon, there are many aspects of the problem that remain obscure. In a few patients the drug can be administered again without producing a recurrence of icterus, and yet in other patients an exquisite hypersensitivity to the agent has been demonstrated.

The histopathology of jaundice due to chlorpromazine is characteristic and represents the typical picture of primary intrahepatic cholestasis. The findings usually observed are centrolobular bile staining, bile casts or plugs predominately centrolobular in location, and minimal evidence of periportal or periductular inflammation. When present, the latter is usually nonseptic in character. The occasional occurrence of some eosinophils scattered among the round cells in the infiltrate lends weight to the concept that the reaction may be allergic in nature.

The laboratory tests in jaundice due to chlorpromazine follow a fairly uniform pattern in the majority of cases. The regurgitation jaundice that occurs is characterized by elevations of both direct and indirect reacting types of serum bilirubin. The degree and duration of the hyperbilirubinemia varies greatly. An increase in the level of the alkaline phosphatase is an almost constant phenomenon; this often precedes the elevation of the serum bilirubin level.[7] The cephalin cholesterol flocculation test, the thymol turbidity reaction, and similar liver tests are usually normal in chlorpromazine-induced jaundice.

Several unusual aspects of the chlorpromazine-induced jaundice problem warrant comment. The occurrence of jaundice some days after the drug therapy has been stopped deserves emphasis. Cases have been described in which jaundice developed 14 to 19 days after chlorpromazine therapy had been discontinued, even though the patient had received the drug for only 5 or 6 days.[8] The diagnosis of intrahepatic cholestasis was confirmed by a liver biopsy secured at the time of operation. In each instance the common bile duct was patent. The apparent late development of jaundice after chlorpromazine therapy has been discontinued has also been witnessed in a patient on the medical service of the University of Minnesota Hospitals. In this instance jaundice was first noted approximately three weeks after the drug was withdrawn. The icterus reached its peak in another three weeks and gradually relented. Icterus lasted approximately two months. The patient was admitted late in the course of the illness, and a liver biopsy was not deemed necessary.

A review of the available liver tests that had been performed indicated the rather characteristic pattern exhibited by patients with chlorpromazine-induced jaundice. Throughout the period of icterus, the bilirubin, phosphatase, and the serum lipid levels were elevated and the cephalin-cholesterol flocculation and thymol turbidity test remained normal. Although the diagnosis was not established with absolute certainty, the clinical course strongly suggested a delayed drug reaction as the cause of jaundice. Such episodes are admittedly uncommon, but they do emphasize the need for a careful inquiry regarding use of recent drugs in all jaundiced patients.

In a few reported instances, jaundice due to chlorpromazine has been very protracted. A remarkable example was reported by Myers and associates.[9] A man, aged 31, developed jaundice and pruritus after receiving the drug for two weeks. He remained jaundiced for 20 months. Five months after the onset of icterus, the patient developed many of the characteristic features of primary biliary cirrhosis, including extensive xanthomata and splenomegaly. Eventually the marked hypercholesterolemia declined and the xanthomata disappeared. Though the patient's jaundice entirely cleared, the spleen remained enlarged and fear was expressed that his cirrhosis might yet progress. Instances of prolonged jaundice due to chlorpromazine have been observed by others. In one reported series,[10] a patient remained jaundiced for 13 months, and a second patient who became jaundiced during early pregnancy remained icteric for eight and one-half months.

I have had an opportunity to see in consultation one patient in whom jaundice lasted for an entire year. The patient received chlorpromazine in the treatment of severe vomiting during the first trimester of her pregnancy. Jaundice developed 17 days after the drug therapy was first started. The patient's jaundice persisted throughout her pregnancy. After an uneventful delivery in December, 1956, the icterus increased in intensity and was followed by a rise in the blood cholesterol level. Fortunately a gradual remission occurred, and by July, 1957, the jaundice had virtually disappeared. Whether or not protracted jaundice is more prone to develop when this form of drug sensitivity occurs during pregnancy is not known. It would seem a wise precaution to discontinue use of the agent very promptly in any pregnant woman receiving chlorpromazine when even a slight rise in the serum phosphatase or bilirubin level indicates the possible onset of this drug reaction.

Jaundice due to Methyl Testosterone.—The clinical and histological observations in patients who have developed jaundice during the course of methyl testosterone therapy have been described by several observers.[11] The following case, studied with other physicians in 1951, illustrates the occurrence of intrahepatic biliary obstruction in a patient who received methyl testosterone orally for a period of four months.

Case 1.—A 54-year-old white man was admitted to the medical service of Drs. Altnow and Bowers at the Eitel Hospital in Minneapolis, March 27, 1951. The patient was referred for study and treatment of jaundice that had been present for one month. The patient had experienced mild indigestion and fatty food intolerance for the preceding two months. Physical examination revealed a deeply jaundiced man; the liver was palpable just below the costal margin. There were no stigmata of cirrhosis present. Routine laboratory studies yielded normal results. The icteric index was 130 units; the prothrombin time was 41% of normal. After a single injection of vitamin K the prothrombin time returned to normal. The stools appeared acholic.

On March 29, a surgical exploration was carried out by Dr. W. I. Nelson. The liver was found to be smooth but deeply bile stained. The gallbladder and bile ducts were collapsed but patent. A T-tube was inserted into the common duct, and a cholangiogram was secured. This revealed that the larger intrahepatic ducts were patent and a free flow of contrast media through the common bile duct into the duodenum was demonstrated. A biopsy of the liver was secured at the operation. Postoperatively small amounts of bile appeared in the T-tube after several days. The patient's jaundice persisted for some time. The T-tube was removed after two weeks.

The liver biopsy revealed bile staining most marked in the center of the lobules. A minimal degree of liver cell damage was apparent in the centrolobular portion where slight disorganization of the cell plates was evident. In general, the architecture of the liver was well preserved. Although numerous bile thrombi were seen, no "bile lakes" were noted. The larger bile ducts were empty. Inflammatory exudate was inconspicuous. The pathologist, Dr. Craig Freeman, termed the lesion an intrahepatic obstruction of unknown etiology. Further inquiries regarding antecedent drug therapy were made. It was learned from the referring physician that the man had received methyl testosterone, 15 mg. per day, from October, 1950, to February, 1951. The medication was discontinued with the onset of jaundice.

Two weeks after operation a series of liver tests was repeated. These were secured during the eighth week of the patient's jaundice, and the results were as follows: serum bilirubin level (one minute) 5.4 and (total) 8.5 mg. per milliliter; cephalin-cholesterol flocculation, negative; thymol turbidity, 1 unit; zinc turbidity, 8 units; serum alkaline phosphatase level, 27.6 King-Armstrong units; serum cholesterol level, total, 298 mg. per 100 ml.; and feces urobilinogen level, 51 mg. per day. The patient's jaundice slowly receded; on May 20, 1951, the total serum bilirubin level was 2.7 and the total cholesterol level, 288 mg. per milliliter. The patient made an uneventful recovery, and the jaundice disappeared by July, 1951. The patient has remained well subsequently.

It seemed evident that this patient developed painless jaundice as a result of intrahepatic cholestasis brought about by a drug hypersisitivity reaction. In most of the reported instances of jaundice associated with methyl testosterone, icterus has appeared after two or three months of therapy. This unusual and admittedly uncommon reaction seems to be limited to patients receiving methyl testosterone; as far as is known it has not been reported in patients receiving testosterone propionate.

Methyl testosterone may be given to relieve itching in patients who have obstructive jaundice.[12] In my experience this usually causes a further rise in the serum bilirubin level. The mechanism by which this agent acts on the liver is unknown. In selected patients with jaundice, methyl testosterone may be administered in an attempt to relieve pruritus, provided such patients are willing to accept the risk of increasing icterus and probable aggravation of any existing tendency toward edema formation. To some patients with intolerable itching this price they must pay for relief of their distress does not seem too high. The following case illustrates the aggravation of the jaundice concomitant with the relief of the pruritus in a patient with secondary (cholangitic) biliary cirrhosis.

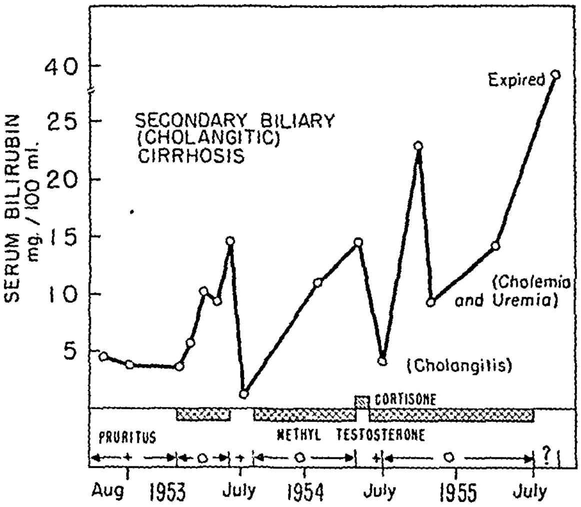

Fig. 1 (case 2).—Jaundice and severe pruritus in patient with biliary cirrhosis. Oral methyl testosterone therapy relieved itching but was accompanied by increase in degree of icterus.

Case 2.—A 69-year-old woman suffered an injury to the common bile duct at the time of a cholecystectomy performed by her private physician in 1950. After a stormy postoperative course the patient developed marked jaundice. Five months later an experienced surgeon operated on the patient and succeeded in anastomosing the right and left hepatic ducts directly to the duodenum. Eighteen months later the patient had an episode of ascending cholangitis. She was first treated at the University of Minnesota Hospitals in August, 1952. After intensive antibiotic therapy and drainage of a right subphrenic space abscess, the patient recovered; low-grade jaundice and intense pruritus persisted. In February, 1953, the patient was given methyl testosterone in amounts sufficient to control her pruritus. This usually amounted to 20 mg. per day.

As shown in figure 1, the patient did obtain relief of her pruritus, but the serum bilirubin level rose. When the drug therapy was discontinued, the jaundice receded and the pruritus returned. These observations were repeated again in 1954. The drug therapy was discontinued in May, 1954, and the patient received cortisone for one month. Although the serum bilirubin level fell, the rate of decline was no faster than previously noted without cortisone. The development of gastrointestinal distress and bleeding necessitated the discontinuing of cortisone therapy. The patient's final year of life was marked by recurrent attacks of cholangitis; this made it difficult to determine how much of the elevation of the serum bilirubin was due to the administration of methyl testosterone and how much to an aggravation of her underlying disease. She eventually developed cholemia and uremia and died.

The case illustrates the aggravation of a preexisting jaundice when methyl testosterone was given to obtain relief of distressing pruritus.

In addition to the agents mentioned, other drugs have been held responsible for the occurrence of jaundice resulting from intrahepatic obstruction. The incidence of such reactions has been far less than with chlorpromazine. The experiences emphasize the need for a careful evaluation of drugs recently administered when one first examines a jaundiced patient. Jaundice due to intrahepatic obstruction resulting from a drug sensitivity reaction may so closely mimic obstructive jaundice produced by gallstone or tumor that the examiner may easily be misled.

An occasional patient with viral hepatitis may exhibit features of prolonged regurgitation jaundice and thus simulate bile duct obstruction. The value of needle biopsy of the liver in establishing the existence of viral hepatitis as the underlying or fundamental disorder in such patients has been recently emphasized.[13] The histopathological changes may not be correctly interpreted unless the specimen is examined by an experienced pathologist who has taken a particular interest in this type of differential diagnosis.

Chronic (Progressive) Forms of Jaundice Resulting from Intrahepatic Obstruction

A classic example of a chronic form of intrahepatic obstructive jaundice is represented in the patient with primary biliary cirrhosis.[14] The victims of this disorder are usually well-developed, well-nourished, middle-aged women who exhibit melanotic pigmentation of the skin. On examination the sclerae are often found to be icteric and the liver enlarged, readily palpable, but seldom tender. The spleen is also enlarged. The skin over the arms and legs, thickened and revealing evidences of self-inflicted scratch marks, attests to the presence of prolonged pruritus. Such patients may or may not exhibit xanthelasma and xanthoma.

The case histories of 30 adult female patients studied at the University of Minnesota Hospitals during the 12-year period 1945 to 1956 have been recently reviewed. In each instance most of the typical features of primary biliary cirrhosis existed. Because of the relative rarity and long duration it is difficult to witness the entire natural course of this chronic disorder in more than a few instances. In the cases reviewed there was no conclusive evidence that a single entity was represented, despite the similar clinical findings exhibited by most of the patients. Nearly all students of the disease have observed its striking predilection for adult women.

The disease often begins so insidiously that it is difficult to determine the onset. This was estimated to be before age 40 in eight instances in the series reviewed; 15 patients appeared to develop the disease between the ages of 40 and 60 years. Three were beyond the age of 60 years when the first symptoms appeared. The exact time of onset could not be determined in four cases. No clear-cut relationship to menses, to pregnancy, or to the menopause was evident. The estimated duration of the disease was from 3 to 16 years in the patients who could be followed.

The existence of primary biliary cirrhosis can be suspected on the basis of the characteristic symptoms of fatigue and pruritus and the physical signs of pigmentation of the skin and enlargement of the liver. It should be emphasized that detectable jaundice may not develop until some time after the onset of the disease. A pathological diagnosis can usually be established during life if an adequate liver biopsy specimen can be obtained. The earliest lesion that can be recognized is a pericholangiolitis, initially associated with bile ductule proliferation. Later the number of bile ductules appears to decrease, and the pathological findings in the liver become increasingly complex as the disease advances.[14]

The etiology of the disease is unknown; MacKay's recent observations [15] offer promise of new insight into this obscure illness. In the majority of instances the disorder appears to be relentlessly progressive once it is established. The late stages are characterized by evidences of portal hypertension and hepatic insufficiency. At present, no specific remedies are known; treatment must be symptomatic and supportive. The clinical management of the patient with primary biliary cirrhosis poses a very difficult problem for the attending physician. In the early phase of the disease, a phase which incidentally may last 3 to 10 years, the problems of the control of itching and fatigue are prominent. In some patients the prolonged elevation of the blood cholesterol level leads to xanthoma formation, with its associated discomfort and disfigurement. As the disorder progresses and slow deterioration of liver function becomes manifest, the elevated blood lipid levels often diminish. The prolonged exclusion of bile from the intestine in some instances may lead to skeletal demineralization. Severe bone pain was noted in three of the patients studied in the present series of 30 cases. Each patient obtained some relief from bone pain when the calcium and vitamin D intake was augmented.

The late phase of the clinical course of primary biliary cirrhosis is marked by the problems of liver insufficiency with edema and ascites formation. Portal hypertension and the occurrence of hemorrhage from esophageal varices is a prominent feature in some instances. The following case has been selected from the series reviewed to illustrate this point and also to emphasize another feature. In assessing the significance of the degree of jaundice in any given patient, it is necessary to consider the total daily pigment production and the excretory ability of the liver. In most of the common forms of cirrhosis, for example, a primarily fatty cirrhosis in an alcoholic patient or an idiopathic postnecrotic cirrhosis in a young woman, an increase in the depth of jaundice usually signifies increasing parenchymal cell damage and is an ominous sign.

In primary biliary cirrhosis, during the early phase at least, the depth of jaundice does not necessarily reflect the same degree of liver cell impairment but rather the inability of the intrahepatic biliary system to excrete the daily bilirubin load. Such patients are barely able to excrete the normal daily load of bilirubin produced by the normal daily rate of red blood cell destruction. If there is even a slight increase in the daily production of bilirubin, i. e., a mild hemolytic process related to the presence of congestive splenomegaly, the degree of jaundice may become quite intense. The depth of jaundice must be considered in relationship to the factors of bilirubin production and the impaired ability of the liver to excrete pigment.

Case 3.—In February, 1955, this 47-year-old woman was referred to the medical service of the University of Minnesota Hospitals because of chronic jaundice, pigmentation, and pruritus. The patient had first consulted a physician in August, 1954; jaundice was observed and bed rest advised on the presumptive diagnosis of hepatitis. There were no known contacts with cases of viral hepatitis in the community, and none had occurred in the family. Six weeks of bed rest failed to produce an alteration in the status of the patient. In October, 1954, she was more thoroughly investigated because the low-grade jaundice persisted. Cholecystography was performed; this revealed a normally functioning gallbladder. A needle biopsy of the liver was interpreted by the pathologist as showing "benign low grade hepatitis." The blood serology report at this time was "V.D.R.L. doubtful positive 1-16" and "Wassermann doubtful positive." The patient's condition remained unchanged despite various measures used.

The admission examination of the patient in February, 1955, revealed an icteric and pigmented woman in no apparent distress save for pruritus. The liver and the spleen were palpable. No ascites was noted. Skin lesions on the legs were considered to be those of lichen planus; this diagnosis was subsequently confirmed by skin biopsy. The patient was closely questioned regarding antecedent jaundice; she admitted that she might have been jaundiced as long ago as 10 years before (at age 37) and the pigmentation and pruritus had begun, insidiously, some time before 1955. The presence of esophageal varices was demonstrated on x-ray examination.

Laboratory studies at the time of this admission revealed the following values: hemoglobin level, 13.3 Gm. per 100 cc.; red blood cell count, 4,300,000 per cubic millimeter; hematocrit reading, 38%; reticulocyte count, 0.5%; white blood cell count, 3,100 per cubic millimeter; and differential count, normal. The results of the liver tests were as follows: serum bilirubin level (one minute and total), 1.3 and 3.7 mg., respectively, per 100 ml.; alkaline phosphatase level, 82 and 45 units (King-Armstrong method) on two studies; cholesterol level, 249 mg. per 100 ml.; cephalin-cholesterol flocculation, 3+; and thymol turbidity, 11 units. The total serum protein level was 7.1 Gm. per 100 ml. (albumin 3.2 and globulin 3.9). The prothrombin time was normal. The fecal urobilinogen level was 507 mg. per day. A bone marrow biopsy disclosed normoblastic hyperplasia and an increased number of megakaryocytes.

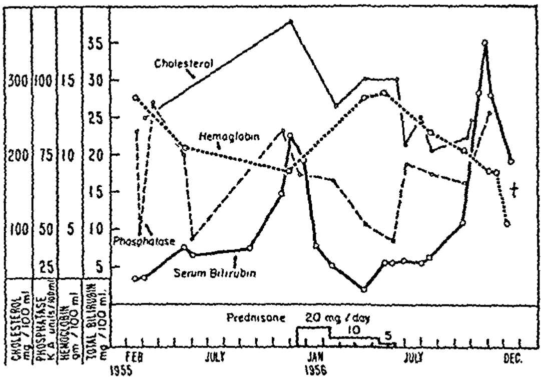

Fig. 2 (case 3).—Primary biliary cirrhosis and hypersplenism. Hemoglobin level rose and bilirubin level declined during period of treatment with steroid. Decrease in jaundice was more likely due to suppression of mild concomitant hemolytic process than to primary effect on liver. Cholesterol level was not significantly affected. Fluctuations in phosphatase levels could not be correlated with any therapeutic agent administered.

Peritoneoscopic examination was performed by Dr. J. B. Carey Jr. The liver appeared coarsely nodular and enlarged. A liver biopsy was reported by the hospital pathologist as indicating "portal cirrhosis." The patient was discharged with a clinical diagnosis of primary biliary cirrhosis and followed in the outpatient department.

The significance of the elevated fecal urobilinogen excretion in the presence of impaired excretory function on the part of the liver was not appreciated. This undoubtedly reflected an increased rate of erythrocyte destruction related to hypersplenism. The patient's condition remained virtually unchanged. Antihistaminics and lotions failed to relieve the pruritus; but except for this discomforting symptom the patient felt well. Her appetite and strength remained satisfactory, and she continued to carry out all of her household duties. In June, 1955, the patient was readmitted to the hospital for a lumbar puncture; the blood serology tests again showed positive results (V.D.R.L., + diluted; Kahn, 3+; Hinton, 4+) in May, 1955. The cerebrospinal fluid was entirely normal, and the spinal fluid (Wassermann) was negative. The treponema pallidum immobilization test, submitted to the Venereal Disease Research Laboratory in Chamblee, Ga., was reported as "nonreactive." In view of the entirely negative evidence for syphilis, the serologic tests were considered to have given biological false-positive reactions. An L.E. clot test was negative at this time.

The physical examination at the time of the second hospital admission revealed no essential change from that observed earlier. The laboratory values remained essentially unchanged (fig. 2); the hemoglobin level had declined somewhat. Although further evidence of hemolytic activity was not sought, the effect of the congestive splenomegaly was suggestive in that the leukocyte count was 2,750 per cubic millimeter, though the differential count was normal. The platelet count was 104,000 per cubic millimeter. The patient was again discharged, and her course was followed in the outpatient department.

As shown in figure 2, the serum bilirubin level gradually rose throughout the 10 months after the patient's original investigations. In December, 1955, the patient was readmitted for the third time for reevaluation. The degree of icterus was intense. The hepatosplenomegaly was again demonstrated. The patient's only complaints were related to pruritus and mild fatigue. The values for the liver tests were similar to those obtained initially. The hemoglobin level was 9.4 Gm. per 100 ml. Evidence of mild hemolytic activity (reticulocyte counts 1.9 and 4.6%) and an elevated fecal urobilinogen level (360 mg. per day) were demonstrated. The leukocyte count was normal (5,200 per cubic millimeter), and a normal differential count was recorded. The platelet count was 184,000 per cubic millimeter.

The administration of prednisone, 20 mg. per day, was begun during this admission, and the patient was discharged on this therapy to be followed in the outpatient clinic. The icterus declined, as can be seen from the values shown in figure 2. Initially, the patient did seem to be somewhat relieved of her troublesome pruritus, although the results were not dramatic. Despite dietary salt restriction the patient experienced fluid retention while receiving steroid therapy. She complained of epigastric distress; this discomfort was only partially relieved by an antiulcer regimen. A search was made for x-ray evidence of an ulcer, but none was demonstrated. In April, 1956, the itching was again as severe as formerly, even though the degree of icterus was greatly decreased. Methyl testosterone, 10 mg. per day, was added to the regimen during May, 1956. This afforded little subjective relief but did aggravate the problem of fluid retention. In June, 1956, prednisone therapy was discontinued. During the ensuing months, several other agents were used in an attempt to relieve the pruritus. They proved ineffectual.

In November, 1955, the patient was admitted to the hospital for the fourth time. The jaundice was again intense, but in other respects the patient's general condition remained relatively satisfactory. Clear-cut evidence of hemolytic activity was obtained at this time in a study conducted by Dr. A. Sigrid Gilbertson. The half-life of the patient's chromium-tagged red blood cells was shown to be only 12 days as compared to a normal of 25 to 30 days. A splenectomy and spleen-renal anastomosis was advised. The patient requested that this be postponed until after the Christmas holidays. This seemed to be a reasonably safe request to grant in view of the apparent well-being of the patient and the chronic nature of her illness. She was permitted to return to her home in rural Minnesota.

Unfortunately the patient experienced a massive hemorrhage from esophageal varices on Dec. 26, 1956. She was subsequently returned to the University Hospital. Despite multiple transfusions and esophageal tamponade the patient continued to bleed massively and remained in a shock-like state. In desperation, an emergency operation was performed and an attempt made to ligate the bleeding esophageal varices by a transthoracic approach. The patient was in a critical condition preoperatively and failed to rally. She died the next day. An autopsy examination revealed cirrhosis, esophageal varices, splenomegaly, ascites, and bilateral hemothorax, most marked on the left side. The spleen weighed 900 Gm. and exhibited congestive changes. The liver weighed 2,540 Gm. and was deeply bile stained and nodular. The gallbladder and bile ducts were normal. Microscopic sections of the liver revealed the characteristic architectural alterations of cirrhosis. The pathologist reported a diminished number of small bile ducts in the fibrous septums. The larger intrahepatic bile ducts were not believed to be abnormal.

This case illustrates a number of features that occur in primary biliary cirrhosis. It is possible that the disease actually began some time before the patient first consulted a physician. The manifestations of the disease were well advanced when the patient was first admitted in February, 1955, since hepatosplenomegaly, pigmentation, and demonstrable esophageal varices already existed. There was suggestive evidence of a slight increase in the rate of erythrocyte destruction even then, though its significance was not appreciated. The slight elevation of the fecal urobilinogen level in a patient with evidence of impaired ability of the liver to excrete bilirubin was such an indication. The slow rise of the serum bilirubin level over a period of the next 10 months (fig. 2) reflected an imbalance between the daily pigment load and the ability of the excretory system to fully meet these demands.

In view of the complexity of such cases it is not at all surprising that the true significance of a gradually rising bilirubin level was incorrectly interpreted and the assumption made that the patient's liver function was seriously decreasing. The trial of steroid therapy was commenced in December, 1955, with the thought that this might possibly reduce the intrahepatic obstruction. In retrospect, the decrease in the serum bilirubin level that occurred between December, 1955, and June, 1956, was more likely due to a suppression of the patient's mild hemolytic activity rather than any primary effect upon the liver. Presumably, the liver was able to cope with a moderate bilirubin load but could not quite keep pace with a moderately increased work load.

The decision to advise a splenectomy and spleen-renal anastomosis should have been reached earlier. It is difficult to advocate a shunting operation as a prophylactic measure in patients with esophageal varices before an episode of bleeding has once occurred. This is especially true in patients with cirrhosis where the operative mortality is appreciable. If the patient survives the first episode of bleeding, the victim and the family are in a much better position to understand the hazards imposed by the presence of varices and the need for taking the necessary operative risk to forestall future episodes. Unfortunately the initial episode of bleeding may prove fatal, as in the case just cited.

In instances of cirrhosis and congestive splenomegaly, consideration should be given to the additional effect of hypersplenism with its attendant hemolytic activity, leukopenia, or thrombocytopenia in the decision regarding prophylactic shunting operations. When a patient with x-ray evidences of esophageal varices exhibits signs of hypersplenism, there may be reason to adopt a bolder attitude and to advise splenectomy and spleen-renal anastomosis without waiting for the first hemorrhage to occur. Admittedly a portocaval anastomosis does effect a greater reduction in portal pressure than does a spleen-renal anastomosis, but in some cases, at least, the congestion of the spleen is not relieved rapidly after a portocaval anastomosis, and the harmful effects of hypersplenism are not promptly eradicated. In selected cases, the removal of the spleen and the performance of a spleen-renal anastomosis may be the operation of choice.

Primary biliary cirrhosis illustrates some additional clinical aspects of intrahepatic obstructive jaundice. It seems important to emphasize that icterus may not necessarily be the first manifestation of the disorder, though the diagnosis is seldom considered before jaundice does appear. In this disease the degree of elevation of serum bilirubin level does not necessarily parallel the degree of parenchymal cell damage as it usually does in other forms of cirrhosis. In such patients, a coexisting hemolytic process related to congestive splenomegaly may greatly exaggerate the degree of icterus.

Summary

The clinical features of jaundice due to intrahepatic obstruction closely simulate those of extrahepatic biliary obstruction. In most instances a correct diagnosis can be made by analyzing the data obtained by clinical, laboratory, x-ray, and histological studies. In some instances operative cholangiography may be required if, after four to six weeks of medical treatment and study, the distinction cannot be made.

Primary intrahepatic cholestasis represents one form of jaundice resulting from intrahepatic obstruction. It is usually a manifestation of a drug sensitivity phenomenon of the type seen in patients who develop reactions to arsenical drugs or chlorpromazine. The intrahepatic obstruction to bile flow is usually self-limited. In rare instances, jaundice may be protracted.

Jaundice due primarily to intrahepatic obstruction (cholestasis) rather than to hepatocellular damage is occasionally seen in patients with viral hepatitis. An experienced pathologist can usually make the correct diagnosis on the basis of a needle biopsy of the liver.

Jaundice due to intrahepatic obstruction is a prominent clinical feature of primary biliary cirrhosis. The rate of bilirubin production (i. e., rate of red blood cell destruction) must be considered in assessing the clinical significance of the degree of icterus at any given time in the course of this progressive disease.

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MECHANISMS OF BILE SECRETION

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The formation of bile in the liver is a complicated process. One group (A) of substances appears in bile in the same concentrations as in blood; this includes glucose and the chlorides of sodium and potassium. A second group (B) appears in bile concentrated as much as hundredfold; this group includes the bile salts, bile pigments, and certain test substances like sulfobromophthalein. A third group (C) is retained in the blood and appears in the bile only in very low concentrations, if at all. Groups A and B are controlled independently of each other, and substances of group B are transferred from blood to bile by an active secretory process. The transfer of sulfobromophthalein involves some active secretion, some storage, and some chemical conversion with other phenomena in addition. Since better understanding of these processes is essential to the interpretation of functional tests and the planning of treatment, further fundamental research is needed.

Bile occupies a peculiar position among secretions: It appears to be somewhere intermediate, from the point of view of its origin, between urine—the result of a sequence of filtration, reabsorption, and secretion—and milk, saliva, or other secretions which spring fully formed from the body of the cells of many typical glands. Understanding of the mechanisms of bile formation has lagged, in spite of a large volume of experimental observations, largely because the pattern of a functional anatomy of the hepatic secretory apparatus has not been established to date. Yet, I believe that enough data have accrued in recent years to justify an attempt at formulating such a picture. This communication will present the results of such an attempted synthesis together with a brief synopsis of the type of experimental material on which my model is based.

Bile is a highly complex composite secretion of widely varying composition. Sometimes this truism if lost sight of, especially in discussions of histopathological material where long-standing usage sanctions the use of the term "bile" to describe the visualization of stainable bile salts or of bile pigments. Many of the difficulties in understanding the pathophysiology of cholestasis can be traced back to this semantic difficulty.

For present purposes, the major bile constituents can be divided into three classes on the basis of the degree of concentration they experience in passage from blood to bile. Class A includes Na^+, K^+, Cl^-, and glucose, with a bile-blood concentration ratio of nearly 1.0; class B includes taurocholates, glycocholates, other bile salts, dehydrocholates, bilirubin diglucuronide, other bile pigments, sulfobromophthalein, fluorescein, rose bengal, and possibly creatinine, with a concentration ratio of 1:10 to 1:1,000; and class C includes alkaline phosphatase, inulin, sucrose, phosphates, and possibly cholesterol, phospholipids, and mucoproteins (plasma proteins, with the exception of alkaline phosphatase, appear not to be represented in the bile), with a concentration ratio of less than 1.0.

This classification can be traced back at least to the experiments of Höber and his school.[1] For the present discussion only classes A and B are relevant. They account for the water and about 95% of the dry matter of bile. Class C poses a series of intriguing but as yet largely unsolved questions and will be left out of the following discussion.

Class A Substances

Class A substances, almost by definition, are transferred to bile in a group, and the rate of their transfer bears no necessary relation to the rate of class B compound secretion.[2] The table lists a few examples in which changes in bile flow rate or composition occur in the absence of corresponding blood composition changes, suggesting that the mechanisms of class A and of class B secretion should be considered as independent of each other in any analysis of bile secretion.

The fact that class A substances as a group appear in bile in concentrations closely reflecting those of plasma has suggested to some that a filtration reabsorption process is the basis of bile volume control. This, however, is incompatible with the experimental facts.

Thus, filtration can be ruled out because bile flow continues up to limiting pressures which, in the isolated rat liver, are always greater than blood pressures.[3] If, furthermore, one takes into account the effective colloid osmotic pressure of the plasma proteins (all but one or two minor ones of which are absent from bile), a pressure differential of such magnitude results that any filtration process can be ruled out a priori. Even a second order con-

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From the U. S. Naval Radiological Defense Laboratory.

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tribution of blood pressures to bile flow rate can be ruled out, since bile flow rates are independent of blood flow or blood pressure whenever the oxygen supply to the tissue is not the limiting factor. This condition can be satisfied at fairly high rates of perfusion at body temperature[3] or over an extreme range of perfusion rates (from 0.3 to 3.0 cc. per gram of liver per minute) either at reduced temperature (30 C) or at elevated oxygen partial pressures (4 atm.).[4]

Active reabsorption also can be eliminated as a factor in bile volume regulation. Under constant blood flow conditions, cooling of the liver results in a sharp fall of bile flow rate—not a rise, as would be predicted from any mechanism dominated by reabsorption. In the rat liver, a 10 C reduction of perfusion temperature reduces bile flow rate by a factor of four between 38 and 18 C.[5] Likewise, ether anesthesia results in a reversible fall of bile flow rate. Thus, it would appear that, in essence, bile formation involves the active transfer of water and possibly of other class A substances from blood to bile.

Examples of Independent Variability of Secretion into Bile of Class A and Class B Components

	Condition	BSP Secretion Rate	Taurocholate Concentration	BSP Concentration Maximum	Bile Flow Rate
Dog (BSP infusion)	Breathing actively	1.30 mg./min.	...	...	98 microliters/min.
	Diffusion respiration (2.5 atm. O_2)	1.07 mg./min.	...	...	38 microliters/min.
Rat (isolated liver)	During 1st hr. of perfusion	...	2.3 mg./cc.	...	1.2×10^{-2} cc./min.
	During 3rd hr. of perfusion	...	0.25 mg./cc.	...	1.0×10^{-2} cc./min.
Rat (isolated liver; 3 mg. of BSP injected)	38 C	...	...	94 mg./cc.	1.5×10^{-2} cc./min.
	30 C	...	...	97 mg./cc.	0.42×10^{-2} cc./min.
Rat (isolated liver)	During steady state	95 mcg./min.	...	...	2.2 cc./min.
	In spontaneous failure	85 mcg./min.	...	...	0.50×10^{-2} cc./min.
Dog (bile fistula)	Continuous BSP (or penicillin) infusion at various rates	BSP (or penicillin) "clearance" rate decreasing sharply with increasing plasma BSP concentration			
	Sodium or lithium chloride by continuous infusion at various rates	Sodium or lithium "clearance" independent of plasma sodium or lithium concentrations			

Further light on blood-bile relations is shed by the study of such other class A components as the monovalent ions Na^+, K^+, and Cl^-. The concentrations of all of these in bile rigorously parallel their concentrations in blood plasma regardless of how much deviation from normal blood levels is seen. In rat bile, potassium concentrations exceed plasma potassium concentrations by about 15%, while sodium and chloride concentrations are very nearly equal in the two phases.[6] This equality of plasma and bile electrolyte concentrations—and osmotic pressures—is preserved even when plasma osmolarity is doubled by the addition of sodium chloride. Bile flow rate, however, is drastically reduced by such a procedure, indicating once again that a cellular phase rather than extracellular equilibrium governs bile flow rate. The location of this cellular phase is suggested in this case by the appearance of watery vacuolation in the hepatic polygonal cells.[7]

The dominant role of the hepatic cells in bile secretion is further confirmed by the observation that in many forms of toxic hepatitis, where bile suppression is among the earliest physiological manifestations, early histopathological changes are confined to these hepatic cells.[8] Thus, transfer of water to bile involves an active, energy-consuming process, is likely to be located at the level of the hepatic cells, and consequently would appear to involve of necessity the transfer of water into the bile capillaries enmeshing these cells.

Once in the biliary tree, bile is not completely isolated from the blood stream. Thus, a net transfer of fluid out of the biliary tree could be demonstrated at elevated bile pressures.[3] The rate of such backflow is dependent on bile pressure: it appears to be nil or very slow, relative to bile secretion at pressures up to about 12 cm. H_2O, and increases very rapidly with further increases in bile pressure until backflow balances secretion rate. This point is the one commonly determined in measurement of so-called bile secretion pressures. Bile composition appears to be independent of bile pressures below 10 or 12 cm. and varies at higher pressures in a manner suggesting interference with the secretory apparatus rather than concentration of bile by selective back filtration.[1] When hepatic venous pressures are elevated at constant portal pressure, it has been found in the isolated rat liver that limiting bile secretion pressures are not similarly raised but either remain constant or decrease slightly. This finding suggests that leakage of bile from the biliary tree under these conditions occurs not at the level of the sinusoidal bed but, rather, hemodynamically close to the entry of the portal blood into the liver, i. e., at the level of the portal areas or even further upstream.

Exchange of electrolytes can occur between bile in passage through the biliary tree and blood plasma. This follows in particular from studies of bile potassium: after radioactive potassium (K^{42}) injection into the blood stream, the specific activity of the large hepatic intracellular potassium pool rises somewhat gradually while bile potassium specific activity has reached the values prevailing in plasma within about one minute.[4] Bile potassium thus is derived from blood and not from the cellular phase of the hepatic parenchyma. The rate of K^{42} appearance, furthermore, suggests that this ion entered the biliary tree pretty well downstream rather than in the canalicular headwaters. Similar results, though less sensitive because of the small sizes of intracellular stores, have been obtained for Na^+ and Cl^-. Together with the above data on the origin of the biliary fluid phase, these data, then, provide the basis for the conclusion suggested above that bile secreted by the hepatic cells in passage down the biliary tree is afforded an opportunity to reach electrolyte equilibrium with the blood plasma. It is tempting to assign this process to the small bile ducts and ductules with their investing vascular plexuses.[9]

Class B Substances

In contrast with class A bile components, those of class B appear in bile in such concentrations that there can be no doubt about the fact that an active secretory process of some kind must be involved in the transfer from blood to bile. Class B compounds share a number of chemical characteristics: they are usually organic carboxylic acids or their salts of molecular weights of the order of 300 or greater, and they share a marked tendency to form complexes with plasma proteins, particularly with plasma albumin. With respect to secretion into bile, also, there are many similarities between these substances, although quantitative differences may exist between them with respect to the degree to which particular properties are displayed. Sulfobromophthalein sodium, an exogenous dye, has had perhaps more study than any other compound from the point of view of its fate in relation to bile secretion. Since, wherever they have been checked, conclusions derived from the study of sulfobromophthalein secretion correspond with observations for other class B compounds, attention here will be focused on this substance as a prototype of the entire class.

Sulfobromophthalein is secreted into bile at concentrations that always far exceed those in the blood stream. Characteristically, however, there is a limiting rate of dye secretion beyond which increasing the dose or the infusion rate of sulfobromophthalein no longer affects the secretion rate; the mechanism involved, whatever its nature, appears to be saturated.

Similar saturation phenomena have been seen for sodium dehydrocholate, bilirubin, and fluorescein[7] and would appear to be characteristic of the biliary secretion of class B compounds in general. Related to this property may well be that of competition for uptake and excretion by the liver, a phenomenon well recognized for the pair dehydrocholate and sulfobromophthalein[10] and recently described also for other pairs, such as bilirubin and sulfobromophthalein and bilirubin and bile salts.[7] A similar mechanism may underlie the inhibition of sulfobromophthalein uptake in the presence of probenecid (Benemid) and of certain shellack suspensions.[7] There is a suggestion in these data that uptake—that is, blood to secretory cell transfer—rather than secretion into bile is involved in these mutual inhibitions.

The path of class B compounds from blood to bile has been explored visually, by tracer methods, and physiologically. By visual observation of fluorescein secretion, Hanzon has demonstrated a sequence of uptake into parenchymal cells, secretion into bile canaliculi, and transport down the biliary tree for this dye.[7] Tracer studies involving sulfobromophthalein labeled with radioactive sulfur (S^{35}) have confirmed and expanded this picture. In the first place, they have proved that blood to bile transport of sulfobromophthalein must involve a cellular phase. Bile in several species does not contain sulfobromophthalein as such but, rather, a series of sulfobromophthalein derivatives together with traces of sulfobromophthalein only.[11] The conversion does not take place in the blood stream, for blood contains mere traces of these sulfobromophthalein derivatives over most of the course of sulfobromophthalein excretion, and the hepatic parenchyma is very active in effecting the conversion. The end product of sulfobromophthalein metabolism in the rat is a phthalein dye, provisionally designated as sulfobromophthalein II, which is secreted without further conversion into bile. The fact that blood-to-bile concentration ratios for this dye, too, are always considerably below 1:1, ranging around 1:10 to 1:50 during continuous infusions in the isolated rat liver, conclusively proves that chemical conversion is not essential to uphill secretion of class B compounds into bile.

Transfer of sulfobromophthalein from blood to bile is not a simple a-to-b process. Even at subsaturation doses, as much as half of the dye entering the cells is stored away.[12] The site of storage appears to be the hepatic cell, both from analogy with fluorescein and on the basis of radioautographic studies. The stored dye is eventually available for excretion into bile. However, maintenance of high secretion rates depends on continued delivery of sulfobromophthalein or of its derivatives to the liver via the blood stream: transferring an isolated liver loaded with sulfobromophthalein or sulfobromophthalein II from the dye-containing circulation to a fresh, sulfobromophthalein-free circulation results in a rapid falling off of dye concentrations in the bile. This behavior is in line with the mode of action of the inhibitors of sulfobromophthalein handling mentioned above.

If S^{35}-labeled sulfobromophthalein II is used in the first and ordinary sulfobromophthalein in the second circulations of such perfusion experiments, the falling off in the rate of excretion of stored up S^{35}-labeled dye after the transfer is virtually the same as though no dye were present in the second system, suggesting that stored sulfobromophthalein and freshly delivered sulfobromophthalein are secreted independently at these dosage levels. That storage and secretion of sulfobromophthalein are somewhat independent processes can also be observed in toxic liver injury; here, secretion of sulfobromophthalein is severely impaired,[12a] while storage remains effective as shown both by direct analysis[12a] and, for the damaged cells, by histological methods.[13] Similarly, in the chick embryo hepatic storage and chemical conversion are demonstrable several days before biliary sulfobromophthalein excretion.[14]

Thus, a complex picture of sulfobromophthalein handling in the liver is gradually emerging, incorporating a storage phase, possible chemical conversion, and secretion as its elements. Anatomic counterparts to these at present can only be derived by analogy with the results of direct observation of fluorescein. As before for water transfer, the parenchymal cell appears to emerge as the central secretory element for class B substances. Rigorous proof of this, however, remains to be furnished.

If the hepatic cell is the primary agent of sulfobromophthalein secretion, the dye thus secreted is delivered into the bile canaliculi which invest the hepatic cells. This conclusion once again is in agreement with Hanzon's in vivo microscopic observations.[7] In passage down the biliary tree, the sulfobromophthalein-laden bile must traverse the zone where plasma-bile equilibration occurs with respect to sodium, potassium, and chloride. In the case of class B substances, however, the rate of exchange must be far slower, since otherwise the very large concentration gradients between blood and bile could not be maintained. Possible evidence for the existence of such exchange may be found in the gradual appearance in plasma of biliary sulfobromophthalein derivatives after sulfobromophthalein injection. In bile stasis, far greater back-transfer is seen both in the blood and in liver lymph,[7] together with recycling which results in accumulation of the end product of sulfobromophthalein metabolism—sulfobromophthalein II in the rat—in the blood and liver; this, however, could represent bulk regurgitation rather than diffusion exchange. The difference in rate of exchange between sulfobromophthalein and similar compounds on the one hand and of K^+ or Cl^- on the other can be reproduced in simple collodion bag dialysis experiments, where the rate constant for sulfobromophthalein exchange is less than one-tenth as fast as that for Cl^- or K^+ exchange at concentrations comparable to those in plasma and bile. Thus, when in a typical experiment sulfobromophthalein concentration inside the bag had decreased from 100% to 80% of the initial value of Cl^- exchange was 92% complete.

Hypothermia affects sulfobromophthalein secretion rates to about the same extent as bile flow.[4] Elevated bile pressures fail to affect bile sulfobromophthalein concentrations until levels are reached where bile backflow assumes important proportions; in that region bile sulfobromophthalein levels may decrease below normal for a given dose. Both these lines of observation confirm the view that selective reabsorption is not a factor in establishing sulfobromophthalein concentrations in bile.

I would like to mention two alternative points of view on sulfobromophthalein handling in the liver. Kupffer's cells were once considered involved in this process on the basis of the effect of India ink on sulfobromophthalein clearance.[15] More recent work has resolved this experiment by the demonstration that something in the suspension medium (the shellack, on most recent evidence) rather than the so-called RE blocking colloid is at the base of the effect and that loading of Kupffer's cells with inert colloid fails to modify sulfobromophthalein handling in the liver.[16]

Again, a most interesting point of view was proposed on the basis of the demonstration of an extensive peribiliary vascular plexus supplied by the hepatic artery; it was proposed that this was an expression of a major functional role of the bile ducts and that this role was the secretion of important bile components, including sulfobromophthalein.[17] As far as the latter assertion is concerned, direct check with use of simultaneous injection of sulfobromophthalein into the portal vein and of S^{35}-labeled sulfobromophthalein into the hepatic artery of dogs has shown either that there are no route-dependent differences in secretion of dye or that the dye introduced into the portal vein is actually secreted preferentially. Thus, the bile ducts do not appear to play a predominant active role in sulfobromophthalein secretion.[18] The peribiliary plexus would, however, appear to be an excellent anatomic device for effecting the exchange between blood and bile constituents described in preceding sections of this paper.

Comment

The following concept represents a useful working hypothesis of the mechanism of bile secretion: Bile flow is initiated by the secretory activity of the hepatic cells. Since, at present, no other single bile component appears to be linked with this process, it seems useful to consider this process as water secretion. Substances of class B are transferred from blood to bile by the same hepatic cells, forming a primary bile in the bile canaliculi.

Primary bile, in passage down the biliary tree, comes into restricted contact with blood plasma. This results in equilibration of Na^+, K^+, and certain other ions and may result in a limited loss from bile of class B components. The difference in exchange rates seems to be largely due to differences in diffusion rates in solution and to differences in ionic radii in relation to the effective pore sizes of the membranes separating blood and bile.

Bulk transfer of bile from the biliary tree to the blood stream can occur when bile pressures are raised. Under such conditions, as well as in the normal liver, selective retention in bile of specific components appears to be of minor importance in determining bile concentration. Anatomically, the peribiliary vascular plexus may represent the area of blood-bile exchange and the juxtasinusoidal extensions of the bile canaliculi,[19] as well as the ductular region,[7] appear likely sites for bulk backflow.

Conclusions

The physiological anatomy of bile secretion, as has been proposed, must be subjected to much further experimental work along such promising lines as the analysis of liver lymph composition, the effects of intermittent or of relative bile stasis, and the ontogeny of bile secretion and its relation to the biochemical and morphological development of the liver. At the same time, I feel that enough background is available to justify preliminary turning of attention to the basic mechanisms which convert the energy provided by biochemical reactions to the physical work of bile secretion. A beginning in this direction has been made in oxygen tension—bile flow studies, in the exploration of enzyme inhibitor effects on bile flow and of the biochemical effects of certain hepatotoxins, in attempts to correlate nutritional studies and bile secretion, and, in particular, in the exploration of the intriguing variety of effects of the several bile flow–stimulating or choleretic agents. This, however, is another tale which, I hope, can be considered in a future discussion.

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CLINICAL NOTES

PERSISTENT SUBARACHNOID-PLEURAL SPACE FISTULA

REPORT OF A CASE

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and
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A fistulous connection between the subarachnoid space of the spinal canal and the pleural space is evidently a rare pathological entity. We have been unable to find a previous account of this condition in the literature. We feel, therefore, that the following case report should be of interest.

A 19-year-old paraplegic man was admitted to the Chicago State Tuberculosis Sanitarium on Oct. 31, 1955, because of a right pleural effusion. The history revealed that he had had no significant illness until 1952, when he received a thoracoabdominal gunshot wound. This wound made an emergency exploratory laparotomy necessary and also was the cause of his present paraplegia. Since the onset of paraplegia he had developed chronic urinary tract infection and decubitus ulcers.

Examination revealed paraplegia of the lower extremities and skin anesthesia from the level of the 10th thoracic segment down. There was a surgical scar on the upper part of the abdomen and a bullet could be palpated in the subcutaneous tissues of the back, near the midline, at about the level of the sixth thoracic vertebra. Breath sounds were impaired in the right lung base.

On Oct. 2, 1955, the patient had developed the pleural effusion while in another hospital. This occurred six weeks after intraspinal alcohol injection, which was given in an attempt to convert the paraplegia from the spastic to the flaccid type. At thoracentesis, 1,800 cc. of clear fluid was obtained. The pleural fluid was negative bacteriologically. The Mantoux test (with purified protein derivative) gave a positive finding in second strength.

Even though there was no bacteriological confirmation of a tuberculous cause, the patient was placed on therapy with streptomycin, aminosalycilic acid, and isoniazid. After eight months of treatment with these drugs, the patient continued to form fluid at a rate requiring removal of 1,000 to 1,500 cc. every two or three weeks. All bacteriological studies of this fluid, including guinea pig inoculations, continued to show negative results. The specific gravity of the fluid was 1.010, the cell count varied from 1 to 3 per cubic millimeter, and the total protein content varied from 1.25 to 1.83 Gm.%. Total cholesterol level was 22 mg.%.

At thoracotomy, 3,500 cc. of straw-colored fluid was removed from the right side of the chest. The pleura was completely normal in appearance except for adhesions along the bullet tract. This appearance was baffling until a minute, dimple-like defect was found in the pleura on the lateral surface of the vertebral column which was exuding small amounts of clear fluid. This defect was probed and found to be a fistulous tract which passed toward the posterior portion of the seventh thoracic vertebra. This tract was unroofed to the point of its termination in the spinal canal, where a small perforation in the dura was discovered. The dura was opened sufficiently to inspect the cord and to make sure no foreign body was present. The dura was then closed with fine silk, and flaps of intercostal musculature and pleura were brought across the site of the fistula to help obliterate it. The parietal pleura was then stripped in the gutter and lateral chest wall to insure subsequent pleural symphysis.

Postoperatively, the patient complained of headaches for about six weeks. This symptom was relieved by lumbar puncture on one occasion. These headaches gradually subsided, and the patient was returned to his original hospital. He has had no recurrence or subsequent complications in a follow-up period of one and one-half years.

Comment

We have presented the case of a paraplegic youth who developed a pleural effusion three years after a gunshot wound which caused his paraplegia. The offending bullet had apparently traversed the right side of the chest, vertebral column, and spinal canal. The pleural effusion developed six weeks after an intraspinal alcohol injection. It was at first presumed to have a tuberculous origin, but after an adequate period of antituberculosis therapy the effusion did not subside and exploratory thoracotomy was performed. This revealed the presence of a fistula between the pleural and subarachnoid spaces.

We are unable to account for the three-year interval between the gunshot wound which produced the fistulous tract and the onset of the effusion. Although the alcohol injection seems to be the only significant event associated with the appearance of the effusion, a causal relationship is not clear.

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From the Chicago State Tuberculosis Sanitarium and the Department of Surgery, University of Illinois.

BLOOD DYSCRASIAS ASSOCIATED WITH TOLBUTAMIDE THERAPY

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During the three years of its use, tolbutamide has established a remarkable record for safety. Side-reactions have been relatively few, consisting of mild gastrointestinal disturbances, skin eruptions, and mild granulocytopenias.[1] These reactions are generally not serious and disappear either after discontinuation of use of the drug or in spite of its continued administration. To date, no serious untoward reactions have been reported. Reactions, however, do occur. It should not be surprising, therefore, if an occasional case should assume grave proportions. With this thought in mind, a case is reported in which serious depression of the bone marrow was observed during the course of treatment with tolbutamide.

Report of a Case

A 69-year-old man was admitted to St. Vincent's Hospital on Aug. 7, 1956, with the chief complaint of weakness and collapse. The history revealed that in 1940 he was hospitalized for rectal abscess and in 1942 for cellulitis of the legs. In 1950, he was found to be hypertensive and suffering from obliterative arteriosclerosis and varicose veins with intermittent claudication. In 1951, a saphenous vein ligation was done; three months later, a sympathectomy on the left side was performed. In 1952, sympathectomy was done on the right. In 1954, he began to suffer from angina pectoris.

Diabetes was detected in 1939 when he was hospitalized for treatment of a rectal fistula. There were no symptoms of diabetes. The diabetes was treated with diet alone for the first year; thereafter, 30 to 35 units of protamine zinc insulin was taken daily. Control of diabetes had been poor due to lack of cooperation. Two years prior to the present illness, the patient changed his attitude and paid close attention to his diet and insulin dosage. Since then, control has been excellent, as manifested by almost normal blood sugar levels, minimal glycosuria, and freedom from hypoglycemic reactions. The weight remained stable. Several blood cell counts during this period were either normal or showed mild degrees of anemia attributed to rectal bleeding from hemorrhoids.

On May 29, 1956, the fasting blood sugar level was 132 mg.%; the urine showed a trace of albumin but no sugar or acetone. His weight was 164 lb. (74.4 kg.). The patient was well and asymptomatic. Therapy with protamine zinc insulin was discontinued.

On June 5, 1956, the fasting blood sugar level was 211 mg.%. A mild postprandial glycosuria was recorded, but acetone was not present. His weight was 159 lb. (72.1 kg.). The patient felt well and was asymptomatic. No insulin was recommended.

History of Present Illness.—On June 19, 1956, the fasting blood sugar level was 279 mg.%; a moderate glycosuria was noted throughout the day but no ketonuria. The patient's weight was 157 lb. (71.2 kg.). He had no symptoms and no complaints. A blood cell count was ordered, and the patient was placed on tolbutamide therapy, 1 Gm. before breakfast and supper. No report on the blood cell count was received.

On June 26, 1956, the fasting blood sugar level was 127 mg.%; there was mild postprandial glycosuria. His weight was 156 lb. (70.8 kg.). There were no signs of hypoglycemia, no symptoms, and no complaints. The evening dose of tolbutamide was reduced to 0.5 Gm.

On July 10, 1956, urine findings were unchanged. The fasting blood sugar level was 162 mg.%. The patient looked and felt well but complained of mild exertional angina in the morning. Tolbutamide dosage was increased to 1 Gm. given twice daily.

During the following weeks, the patient did not return for weekly check-ups as was advised. When he appeared again on Aug. 7, 1956, he was pale. He reported that for three weeks he had felt weak and had collapsed several times. He blamed the tolbutamide for his symptoms and stopped taking it, but he did not resume insulin therapy. When he did not notice any improvement, he returned to the clinic.

The urine showed glycosuria but no ketonuria. He was admitted to the hospital. Physical examination showed his weight to be 154 lb. (69.9 kg.), temperature 98 F (36.6 C), pulse 80 per minute and irregular, blood pressure 140/76 mm. Hg, and respiration rate 20 per minute. The lungs showed crepitant rales at both bases. The heart was slightly enlarged, and a faint systolic murmur was heard over the apex. There were operative scars on the lower extremities. The feet were cool, and the pedal pulses were not palpable. The tendon reflexes were absent in the lower extremities. Chest x-ray showed cardiac enlargement, pulmonary congestion, and a small pleural effusion on the right side. The electrocardiogram showed atrial fibrillation with a left ventricular strain pattern. The blood cell count was as follows: hematocrit value, 20%; hemoglobin level, 5.8 Gm.%; red blood cell count, 2,300,000 per cubic millimeter; and white blood cell count, 2,200 per cubic millimeter, with reticulocytes 0.6%, polymorphonuclears 43%, lymphocytes 48%, monocytes 4%, and platelets 80,000 per cubic millimeter. Bone marrow revealed sparsely cellular marrow with relative hypoplasia of the myeloid and relative hyperplasia of the erythroid series.

The patient was given blood transfusions. The diabetes was promptly controlled with diet and insulin and the cardiac decompensation corrected with digoxin and diuretics. Attempts to improve the blood dyscrasia with vitamin B_{12}, liver extract, iron, and steroids were unsuccessful. The patient was kept comfortable by repeated transfusions. He was discharged on Aug. 29, 1956, and advised to return at stated intervals for reevaluation. Repeated bone marrow examinations were done during his stay in the hospital but revealed no significant change.

The patient was readmitted to the hospital on Sept. 11, 1956. Except for the absence of congestive failure the physical findings were unchanged. The vital signs were normal. The laboratory data revealed blood urea nitrogen level, 20 mg.%; creatinine level, 2.5 mg.%; hemoglobin level, 6.4 Gm.%; red blood cell count, 2,400,000 per cubic millimeter; and white blood cell count, 2,600 per cubic millimeter, with polymorphonuclears 40%, eosinophils 2%, monocytes 1%, lymphocytes 57%, and platelets 61,000 per cubic millimeter. Repeated blood cell counts at weekly intervals revealed no significant changes.

The patient was given blood transfusions. A second trial with the above-mentioned hematinics proved equally unsuccessful. The patient remained fairly comfortable until Oct. 9, 1956, when he experienced a moderate sustained fever and signs of pneumonia at both lung bases. Tetracycline (Achromycin) was given, and the temperature returned to normal after four days. On Oct. 16, 1956, the patient, while sitting quietly in a chair, suddenly fell over and died.

Autopsy was performed on Oct. 18, 1956, by Dr. Julia Miyares. A brief summary of the findings is as follows: arteriosclerotic heart disease with coronary artery sclerosis; segmental narrowing and subintimal hemorrhage of the left anterior descending coronary artery; and subendocardial and subepicardial petechiosis of the myocardium. The lungs showed confluent lobular pneumonia, involving the right

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From St. Vincent's Hospital.

middle and left lower lobe with a small caseous tubercular focus in right upper lobe. The pancreas was the site of mild hemorrhagic peripancreatitis. The bone marrow revealed marked hypoplasia of the granulocytic, megakaryocytic, and erythroid series. The features were those of severe hypoplasia.

Comment

It may well be said that conclusive proof for causal connection between tolbutamide therapy and the blood dyscrasia has not been established since there is no record of a blood cell count immediately preceding use of the drug. Against this contention, however, are the following facts: For quite some time before and for at least three weeks after the use of tolbutamide, the patient felt well, looked his usual self, and had no complaints except that of occasional mild angina, which he had been having for over two years. Search of his records for over four months prior to his anemia failed to reveal any suggestive complaints or use of other medication. The patient himself denied taking any medicine, nor could any history be elicited that indicated exposure to other toxic agents. The patient's history and the blood findings in August, 1956, are compatible with the suggestion that the onset of the dyscrasia occurred shortly after the beginning of the use of tolbutamide. Certainly, the consideration of the possibility of a causal connection between the drug and blood findings appears justified.

Summary and Conclusions

Severe, protracted, and probably lethal aplastic anemia occurred in a patient taking tolbutamide. This should in no way discourage the use of this effective and generally remarkably safe drug. It should, however, remind the physician of the possibility that mild and inconsequential reactions may occasionally assume grave proportions and alert him to the necessity of detecting them by frequent blood cell counts early in the course of treatment.

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LEG ULCER IN RHEUMATOID ARTHRITIS

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Rheumatoid arthritis has many visceral manifestations which serve to emphasize the systemic nature of the disease. Lesions have been reported in the nerves, muscles, heart, brain, eye, bones, gastrointestinal tract, pleura, lungs, and larynx.[1] This paper presents the clinical and histological findings in a patient with a leg ulcer in rheumatoid artritis.

Report of a Case

A man, aged 52, was admitted to the Arthritis Clinic on Feb. 2, 1957, with a history of rheumatoid arthritis since 1946. He was thin and pale. The hip joints, right knee, ankles, and right elbow and wrists were swollen and tender. The adjacent muscles were conspicuously wasted. The proximal interphalangeal joints showed characteristic "spindling" deformities, and the fingers were deviated to the ulnar side. There was a poor response to therapy with gold salts, prednisone, prednisolone, and triamcinolone in large doses. Facial roundness was evident, and he had a palpable spleen. The blood hemoglobin level was 11 Gm. per 100 cc.; the white blood cell count was 4,200 per cubic millimeter, with 65% polymorphonuclear neutrophil leukocytes; and the erythrocyte sedimentation rate (Westergren) was 55 mm. in the first hour. The latex fixation test gave a positive result. The serum uric acid level was 2.5 mg. per 100 cc. The L. E. cell test and Wassermann test showed negative results. The temperature was 99 F (37.2 C) and blood pressure, 130/90 mm. Hg. The heart showed a moderate degree of left ventricular hypertrophy. Subcutaneous nodes (3 cm. in diameter) were found over both olecranon processes.

In April, 1957, he suddenly developed a painful ulcer in the posterior lower third of the right leg. It measured 4 by 5 cm. and was 0.5 cm. in depth (fig. 1). The ulcer was similar to those previously reported.[2] The margins were sharply demarcated with a typical punched-out appearance. There was little discharge, with minimal inflammatory reaction in the surrounding tissue. A greyish exudate was evident at the base of the ulcer. The pain was very distressing. My interest was intensified by the fact that this lesion did not respond to routine and accepted measures of therapy. There was no evidence of varicosities, no deep or superficial venous thrombosis, no diabetes mellitus, no evidence of infection, and no edema. Repeated cultures showed no pathogenic organisms. Complete bed rest with elevation of the foot of the bed had no effect. Prolonged local and general antibiotic therapy, steroids, gold salts, phenylbutazone, trypsin (Parenzyme), streptokinase-streptodornase (Varidase), ultraviolet rays, sulfonamides, and flexible adhesive bandage were unsuccessful.

A specimen of tissue from the ulcerated area showed three distinct features: a zone of necrosis and fibrinoid alteration; an intermediate zone characterized by palisading of histiocytes and young fibroblasts with infiltration of small round cells; and an outer zone of fibrous tissue with numerous blood vessels (fig. 2). These histological characteristics are in accord with the typical lesion of the rheumatoid nodule described by Klinge[3] in 1933 and are considered to be pathognomonic.

With large doses of methylprednisolone, this patient experienced a dramatic relief from pain and stiffness as well as a decrease in all the objective signs of joint disease. The subcutaneous nodules rapidly lost their tenderness and diminished in size. Withdrawal of the drug was followed by a rapid increase in the size and tenderness of the subcutaneous nodules. The leg ulcer, however, demonstrated no change during steroid therapy. This feature has been previously recorded in similar patients and was of considerable interest.[2]

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Comment

Although rheumatoid disease has previously been described in practically all of the viscera, the precise site and the histological appearance of the leg ulcer has not been clearly defined. In a recent report of 200 leg ulcers, 150 were classified as varicose, 30 as post-thrombotic, and 20 as miscellaneous.[4]

Edema was considered to be the final cause in all three groups. The edema was due to the failure of weakened or poorly used calf muscles to maintain an adequate venous return (e. g., hemiplegia, rheumatoid arthritis, arthritis of hip and knee).

The leg ulcer reported here was very painful and was not relieved by rest. It presented a typical punched-out appearance with very little drainage. It occurred in the lower third on the posterior aspect of the leg and did not respond to conventional therapy. (The original hypothesis of edema as the cause did not provide a satisfactory explanation.)

Not all patients with rheumatoid arthritis develop leg ulcers. It is plausible that trauma may play an important etiological role. Two ulcers of this type have been observed to heal with no specific type of therapy.

Whether the connective tissue is a prime reactor in rheumatoid disease or is involved secondarily, Gross [5] believes that the crippling deformities and much of the functional impairment result from failure of the newly forming connective tissue to reproduce the normal structures. Although this healing phase may be nonspecific, it is a major feature of the course and ultimate consequence of this disease. In his opinion, there is little evidence as yet that collagen is involved in any way other than as an innocent bystander or in the healing of accompanying injury. Fibrinoid has long been considered the hallmark of connective tissue diseases and yet may be nothing but the end-result of a relatively nonspecific process. It may be recalled that the cause and cure of scurvy, a connective tissue disease, are known, but the biochemical functions of vitamin C are still unknown.[5]

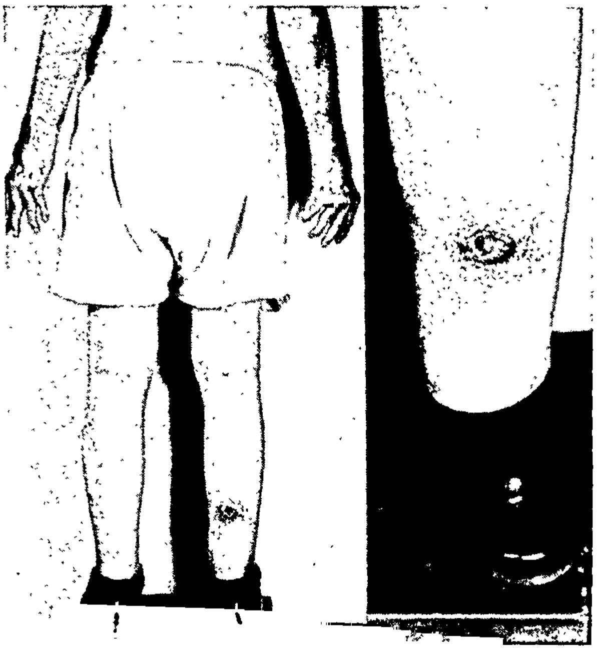

Fig. 1.—Leg ulcer in patient with rheumatoid arthritis.

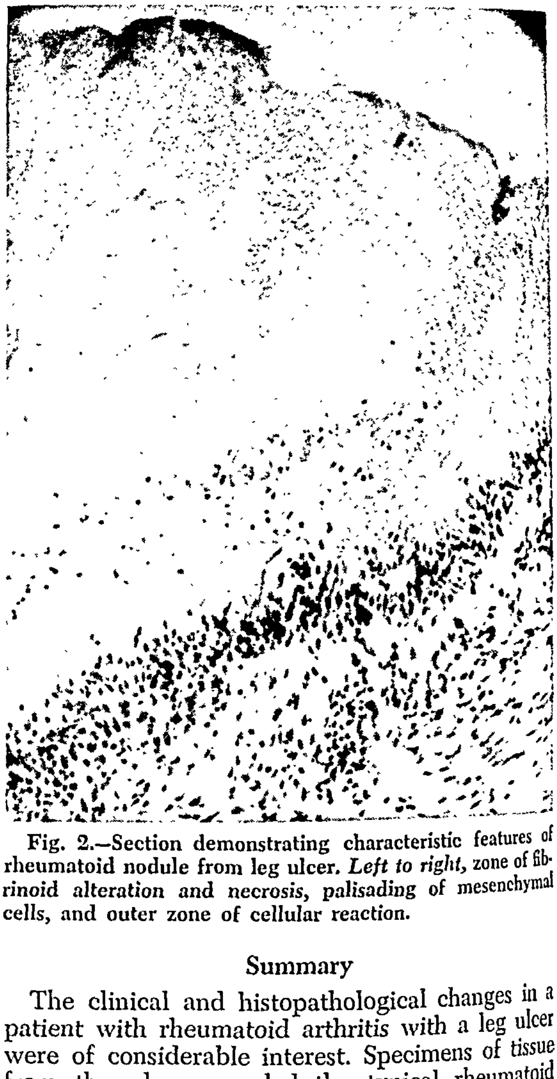

Fig. 2.—Section demonstrating characteristic features of rheumatoid nodule from leg ulcer. *Left to right,* zone of fibrinoid alteration and necrosis, palisading of mesenchymal cells, and outer zone of cellular reaction.

Summary

The clinical and histopathological changes in a patient with rheumatoid arthritis with a leg ulcer were of considerable interest. Specimens of tissue from the ulcer revealed the typical rheumatoid nodule. The lesion did not disappear with any routine therapy, including that with large doses of corticosteroids. The clinical course in a case previously observed followed a similar pattern.

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Dr. G. Silverman did the biopsy studies and M. Pikuritz supplied the illustrations.

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SPECIAL ARTICLE

HISTORY OF THE SECTION ON OBSTETRICS AND GYNECOLOGY OF THE AMERICAN MEDICAL ASSOCIATION

Woodard D. Beacham, M.D., New Orleans

I am grateful for the honor of your addition of my name to the roster of obstetricians and gynecologists who have occupied the chairmanship of this section, and I appreciate the opportunity of presiding at its 94th meeting. I was tempted to prepare a Chairman's address concerning the misuse of words in our discipline. For example, when one really means "nullipara" he should not say "primipara." However, consideration of philosophical subjects and reports of progress in our specialty required me to seek a complete list of the titles of addresses of my predecessors. When it became evident that no such record was available, the title chosen offered its challenge.

1847 to 1876

At the first meeting of the American Medical Association in May, 1847, in Philadelphia, Nathaniel Chapman served as President. In that year Sir James Simpson introduced chloroform anesthesia in obstetrics, Semmelweis demonstrated the role of antisepsis in the prevention of puerperal fever, and Carl Ludwig invented the kymograph. Six years prior Oliver Wendell Holmes had written his paper on puerperal sepsis.

At the meeting held a year later in Baltimore, the Committee on Obstetrics reported "the anesthetic agents ether and chloroform have now been used in perhaps 2,000 cases of midwifery, and so far as the committee have been able to learn without a single fatal, and few, if any, untoward results."

In 1859 a Section on Practical Medicine and Obstetrics was authorized following a report introduced by J. B. Lindsley of Tennessee, who was chairman of the committee appointed to inquire into the propriety of dividing the Association into sections for the better performance of its work (see table).

The 1860 meeting of the Section on Practical Medicine and Obstetrics was called to order by N. S. Davis, of Chicago, and Amos Nourse was elected the first Chairman of the Section. In his A. M. A. presidential address, Henry Miller brought out openly the question of illegal abortion and urged action by legislatures in every state against this practice. The 1861 and 1862 meetings were canceled because of the Civil War. The following year there was a meeting in Chicago without sections.

In 1864 the A. M. A. met in New York City without Southerners and Nathan Smith Davis, founder of the A. M. A., was elected President. Fordyce Barker, who was Chairman of the Section on Practical Medicine and Obstetrics, later became the first President of the American Gynecological Society. The Secretary wrote: "several hundred members being present during the course of the meeting." Papers read included "Death from Air in the Circulation Introduced Through the Uterine Sinuses"; "A Modified Ring Pessary for the Treatment and Cure of Anteflexion and Anteversion of the Uterus"; "On the Use of Pessaries"; and "The Relations of Female Patients to Hospitals for the Insane: The Necessity on Their Account of a Board of Consulting Physicians to Every Hospital."

At the third meeting Zina Pitcher, who served as the 10th President of the A. M. A. and was thrice mayor of Detroit, occupied the chairmanship. H. R. Storer, of Boston, was awarded the A. M. A. gold medal for his essay entitled "The Criminality and Physical Evils of Forced Abortions." In the Section's minutes it is recorded that the Secretary commenced to read the paper of an absent member and, after the expiration of more than an hour, a motion was made to suspend its further reading and it was referred to a committee.

The program of the fourth annual meeting contained no obstetrics. There was a "Report of the Committee on Diphtheria as It Has Occurred in the United States" and one on "So-called Spotted Fever."

At the 1867 session the designation was the Section on the Practice of Medicine and Obstetrics. Included in the program was a paper entitled "Extra-uterine Foetation and Gestation, and the Early Signs Which Characterize It: Symptoms of the Fatal Hemorrhage into the Peritoneal Cavity, Its Usual Termination: Suggestions for the Positive Diagnosis of This Fatal Condition, and a Plan for the Treatment Indicated in It, with a View of

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From the Department of Obstetrics and Gynecology, Tulane University School of Medicine.

Chairman's address, read before the Section on Obstetrics and Gynecology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

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		M. K. Taylor, Keokuk, Iowa
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New Orleans	1869	H. F. Askew, Wilmington, Del.
Washington, D. C.	1870	Joseph Kammerer, New York
San Francisco	1871	H. R. Storer, Boston
Philadelphia	1872	D. A. O'Donnell, Baltimore
St. Louis	1873	D. A. O'Donnell, Baltimore
Detroit	1874	Theophilus Parvin, Indianapolis
Louisville, Ky.	1875	W. H. Byford, Chicago
Philadelphia	1876	S. C. Busey, Washington, D. C.
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> Recent writers, with few exceptions, teach the entire inefficiency of any form of treatment for the cure of intramural fibrous tumors of the uterus except by enucleation, and this operation is so dangerous and difficult as not to be thought of except in desperate conditions. . . . I conclude my address with the cautionary observation that ergot in the treatment of fibrous tumors of the uterus is a prompt and very powerful agent which cannot be recklessly used without great danger; and that much careful observation is still necessary to enable us to determine the circumstances under which its administration will be both safe and effective.

Marion Sims was the Independence Centennial Jubilee A. M. A. President. S. C. Busey served as the Section Chairman and related, "The written law of this Association limits this address to the discussion of the 'advances and discoveries of the past year,' in obstetric, gynesic and pediatric medicine. However willing or competent I might be to fill the measure of this requirement, the time allowed me would necessarily preclude a critical examination of all the contributions to this department. Nor would this be desirable, since many of them are mere novelties of little or no value, or hasty promulgations of immatured opinions and illogical conclusions." He then proceeded to give an excellent review of the recent literature and lists some 81 references. Referring to an article on the substitution of electrolysis for ovariotomy he said, "So successful has this method proven in the practice of Dr. Semeleder that I hesitate to accept his statement, and am startled at the thought that the greatest triumph of modern surgery is to be superseded by a process so simple and so painless."

1877 to 1887

Chairman James P. White referred to some of the "advances and discoveries of the past year" in his 1877 address. He spoke highly of and predicted a great future for the American Gynecological Society, founded in September of the preceding year. He stated, "In conclusion, I beg to call the attention of this Association to the great neglect on the part of the schools in clinical teaching in obstetrics, and in the diseases of the generative organs. There is no subject in the whole college curriculum which so imperatively demands bedside observation as the process of parturition."

In 1878 Edward W. Jenks spoke on "The Causes of Sudden Death of Puerperal Women," listing numerous references, including one to "the late Professor Charles D. Meigs," who in 1849 in the *Philadelphia Medical Examiner* directed "attention to the possibility of spontaneous coagulation of the blood in the right side of the heart and pulmonary arteries as a cause of death in the puerperal state." In conclusion he stated that the mortality due to puerperal convulsions during the last 20 years had been reduced from 32 to 14% and said, "This is but one illustration of what has been done by our science and art in the past, but it is a significant prophecy of what we may expect in the future."

Chairman Ernest S. Lewis, in 1879, discussed "Abdominal Palpation," "Antiseptic Management in Labor," "Puerperal Fever," "Laparo-elytrotomy," "Primary Conversion of Occipito Posterior into Occipito Anterior Position," "Post Partum Hemorrhage," and advances and progress in "Gynecic-Surgery," including "Censure and Condemnation of Total Extirpation of the Uterus in Cancer," and quoted the brilliant successes of Freund and Schroeder in surgical treatment of cancer. He included a section on "Uterine Fibroids" in his address.

The 1880 Chairman was absent; consequently, G. M. B. Maughs, of Missouri, served pro tem. The Section dropped "and Children" from its name so that it became known as the Section on Obstetrics and Diseases of Women. Papers given included "Battey's Operation in Epileptoid Affections"; "The Management of the Third Stage of Abortion, with Retention of Placenta and Membranes"; and "A Clinical Contribution to the Subject of Removal of the Uterus, in Whole or in Part, for the Extirpation of Tumors Connected with That Organ."

James R. Chadwick chose as his title "Obstetrics and Gynaecological Literature, 1876-1881." He mentioned that the *American Journal of Obstetrics and Diseases of Women and Children* was first published in 1869. He also listed the titles of other periodicals devoted to obstetrics and gynecology published in America and in eight other countries, with dates founded. One table was labeled "Analysis of the Literature of the Year 1880 by Nationalities."

The next Chairman was H. O. Marcy, A. M. A. President 10 years later, who discussed "Fibroid Tumors of the Uterus." He stated, "The peritoneal cavity is no longer the *terra incognita* of the surgeon, nor its invasion attended with the fears or dangers of even a very recent period." He said the growths should be classified as myomas and discussed the various methods of treating them in his thorough and comprehensive presentation.

1883 was the birth year of THE JOURNAL of the American Medical Association. Chairman J. K. Bartlett's address, "Topics in Gynecological Surgery," included discussion of "Extra Uterine Pregnancy," for which he recommended galvanism over faradism. He also advocated its use in such conditions as "Dysmenorrhea" and "Post Partem Hemorrhage."

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Chairman James P. White referred to some of the "advances and discoveries of the past year" in his 1877 address. He spoke highly of and predicted a great future for the American Gynecological Society, founded in September of the preceding year. He stated, "In conclusion, I beg to call the attention of this Association to the great neglect on the part of the schools in clinical teaching in obstetrics, and in the diseases of the generative organs. There is no subject in the whole college curriculum which so imperatively demands bedside observation as the process of parturition."

In 1878 Edward W. Jenks spoke on "The Causes of Sudden Death of Puerperal Women," listing numerous references, including one to "the late Professor Charles D. Meigs," who in 1849 in the *Philadelphia Medical Examiner* directed "attention to the possibility of spontaneous coagulation of the blood in the right side of the heart and pulmonary arteries as a cause of death in the puerperal state." In conclusion he stated that the mortality due to puerperal convulsions during the last 20 years had been reduced from 32 to 14% and said, "This is but one illustration of what has been done by our science and art in the past, but it is a significant prophecy of what we may expect in the future."

Chairman Ernest S. Lewis, in 1879, discussed "Abdominal Palpation," "Antiseptic Management in Labor," "Puerperal Fever," "Laparo-elytrotomy," "Primary Conversion of Occipito Posterior into Occipito Anterior Position," "Post Partum Hemorrhage," and advances and progress in "Gynecic-Surgery," including "Censure and Condemnation of Total Extirpation of the Uterus in Cancer," and quoted the brilliant successes of Freund and Schroeder in surgical treatment of cancer. He included a section on "Uterine Fibroids" in his address.

The 1880 Chairman was absent; consequently, G. M. B. Maughs, of Missouri, served pro tem. The Section dropped "and Children" from its name so that it became known as the Section on Obstetrics and Diseases of Women. Papers given included "Battey's Operation in Epileptoid Affections"; "The Management of the Third Stage of Abortion, with Retention of Placenta and Membranes"; and "A Clinical Contribution to the Subject of Removal of the Uterus, in Whole or in Part, for the Extirpation of Tumors Connected with That Organ."

James R. Chadwick chose as his title "Obstetrics and Gynaecological Literature, 1876-1881." He mentioned that the *American Journal of Obstetrics and Diseases of Women and Children* was first published in 1869. He also listed the titles of other periodicals devoted to obstetrics and gynecology published in America and in eight other countries, with dates founded. One table was labeled "Analysis of the Literature of the Year 1880 by Nationalities."

The next Chairman was H. O. Marcy, A. M. A. President 10 years later, who discussed "Fibroid Tumors of the Uterus." He stated, "The peritoneal cavity is no longer the *terra incognita* of the surgeon, nor its invasion attended with the fears or dangers of even a very recent period." He said the growths should be classified as myomas and discussed the various methods of treating them in his thorough and comprehensive presentation.

1883 was the birth year of The Journal of the American Medical Association. Chairman J. K. Bartlett's address, "Topics in Gynecological Surgery," included discussion of "Extra Uterine Pregnancy," for which he recommended galvanism over faradism. He also advocated its use in such conditions as "Dysmenorrhea" and "Post Partem Hemorrhage."

The next year Thaddeus A. Reamy said, "The editorial criticisms of new doctrines, discoveries, methods, or operations are generally from the pens of those who, by education and special training, have superior abilities for such work. It is, therefore, deemed appropriate on the present occasion, to refer you for an 'Annual Report on Obstetrics and Diseases of Women' to these more fertile and instructive sources . . . . Craving your indulgence, I beg to offer, in lieu of such an address, 'Notes on Two Hundred and Thirty-One Cases of Operation for Laceration of the Cervix Uteri.'" He included discussion of the possibility of cancer originating in lacerations.

R. S. Sutton, M.D., LL.D., in "A Brief Review or the Growth of McDowell's Operation Done at Danville, Kentucky, in 1809: Its Present Status," emphasized that the solitary exception to the original procedure at the end of almost three-quarters of a century was that the ends of the pedicle ligature were being cut short. He eulogized J. Marion Sims, who died in 1884.

S. C. Gordon spoke on "Hysteria and Its Relation to Diseases of the Uterine Appendages." His advocacy of surgery was strong. Although he stated that it was impossible in a majority of cases to determine by touch diseases of organs that produce symptoms, he said that the specimens removed were usually severely pathologically altered.

After stating, "The past year has given few, if any, remarkable discoveries, either in gynecology or obstetrics," F. M. Johnson proceeded to discuss "Ovariotomy," "Hot Water in Shock," "Cocaine in Gynecology," "Caesarean Section" (on which he looked with favor, especially the Sanger-Leopold operation), and "New Pathology in Labor," in which he stressed the etiological relationship between pregnancy and kidney disease, with theories on eclampsia.

1888 to 1899

Chairman Ely Van De Warker spoke on "How Gynecology Is Taught," at the 1888 meeting. The Society Proceedings of the A. M. A. disclose that amendments were offered by H. N. Moyer, including: "The Section of Surgery shall hereafter be denominated the Section of Surgery and Gynecology. The Section on Obstetrics and Diseases of Women shall be abolished. The Section on Diseases of Children shall hereafter be denominated the Section of Obstetrics and Paediatrics."

Under Domestic Correspondence in The Journal of the American Medical Association, June 8, 1889, there is an unsigned letter entitled "Shall the Section of Obstetrics and Diseases of Women Be Abolished?" which emphasized "both the study and practice of obstetrics and gynecology must remain so correlated that they can only be successfully cultivated conjointly. To abolish this Section of the Association, now so successfully conducted, would scatter the members into other crowded Sections, and do the cause of science and the Association serious injury." The official report of the next meeting, which was held in Newport, R. I., appears in The Journal, July 20, 1889, revealing that a motion to lay the proposed amendments on the table and indefinitely postpone was carried by a large majority. W. H. Wathen presided at the Section meeting, speaking on "Pathology of Ectopic Pregnancy and Pelvic Hematocele."

Chairman William Warren Potter, who was the first secretary of the American Association of Obstetricians and Gynecologists (1888), spoke on some advances during the previous year and suggested that the By-Laws be amended to create a vice-chairmanship, the Secretary's tenure be longer than a year, and the proceedings be published in a separate volume, including stenographic reporting of discussions. Tarnier's traction forceps were referred to as "ingenious and useful." Potter quoted the mandate of the Apostle, "Prove all things; hold fast that which is good."

C. A. L. Reed, the 53rd A. M. A. President, was the 1891 Chairman. Although the *Transactions of the Section on Obstetrics and Diseases of Women* commenced that year, they do not include an address by him, nor have we found it elsewhere. In his biography by Walter L. Bierring, we find him described as "one of the most interesting and dynamic figures in American medicine." The program included "Relation of Gynaecology to Neurology"; "Rapid Dilatation and Curetting"; "Pathological Anteflexion of the Uterus"; Practical Experience in the Treatment of Accidental Abortion"; "Prevention of Puerperal Eclampsia by the Induction of Premature Labor"; "The Operative Treatment of Extra-uterine Pregnancy at or Near Term, with Report of a Case"; and "Extra-uterine Pregnancy."

E. E. Montgomery presented an address on "Some Mooted Points in Obstetrics and Gynecology" the following year. He advocated Braxton Hicks version in cases of placenta previa, reporting a fetal mortality of 70 to 80% and a maternal mortality of 6 to 7%. In discussing "hysterectomy versus supra vaginal hysterectomy in fibroid growths," he recommended total hysterectomy. He referred to two cases of hysterectomy done through sacral resection "with gratifying results."

John Milton Duff gave no formal title but made general references to the objectives of the meetings. Regarding the work of the previous year, he reported it "not characterized by much that was unique or peculiarly brilliant and original." He advised early and prompt therapy for placenta previa, stating that watchful expectancy is "utter absurdity." For puerperal infection he recommended asepsis with early and vigorous treatment, stating that the death rate (2½%) was declining.

In his oration on suprapubic hysterectomy as viewed from the standpoint of personal observation and clinical research, Chairman Joseph Eastman said:

> The century which in a few years will have rolled on to the eternal past, has placed in the magnificent temple of medicine many pillars of surpassing beauty and grandeur, while its surgical columns have risen high toward Heaven where as gilded towers, they fain would vie with the God-given sunshine in dispelling the chill and gloom of human agony.
>
> Chirurgia's tower, thy lights resplendent blaze
> Dries woman's tears, and lengthens out her days;
> McDowell and Sims of our Columbia's clime
> Began the work moved onward nigh sublime.
> To women, then, these blessings shall be given—
> Queen of the home and home the type of Heaven.
>
> Abdominal surgery is *proud* of her past because it is prophetic of her *future*. Even now in the vital present it shall stand forth unchallenged as the crowning glory of all science and of all art.

F. H. Martin's address was on "Some Mooted Points in Pelvic Surgery." He used galvanism in "desperate" cases but said, ". . . in the present state of pelvic and abdominal surgery, I would not voluntarily administer or recommend Galvanism for fibroid tumors, the subjects of which were under 40 years of age, whose tumors were suitable for operative procedures, and whose general health would show an average chance for favorable surgery." He favored hysterectomy instead of removal of the appendages for fibroids, discussed vaginal ligation of the broad ligament to check uterine hemorrhage and to cause atrophy of uterine tumors, stressed the importance of renal evaluation prior to surgery, and recommended silk and antiseptic absorbable ligatures for intra-abdominal operations. He was the first secretary-general of the American College of Surgeons, being one of its founders in 1913.

Joseph Taber Johnson keynoted his remarks on "Puerperal Infection" by emphasizing prevention, namely, "cleanliness and ventilation." He favored the treatment of Lush of New York, who stated, "The more these cases are let alone and the more simple the treatment the more likely they are to get well." He declared, ". . . when the placenta is praevia the uterus should be emptied," as there is "no wisdom or safety in delay." When the cervix was dilated, Braxton Hicks method was advocated. He advised hysterectomy for control of hemorrhage. He gave his reasons for favoring vaginal hysterectomies as "completeness, drainage, avoidance of shock by less handling of intestines, less peritoneal infection, no abdominal wound, and less liability to hernia." In closing he said, "The present Chairman hopes that his successor may be able to report good developments and improvements in the diagnosis of abdominal and pelvic diseases of women, from the evolution of 'x-rays' about which we have heard so much of late. If its promises are fulfilled we ought to find little difficulty hereafter in our diagnosis of extra uterine pregnancy, pyosalpinx, fibroid, dermoid or ovarian tumors."

Milo B. Ward, who occupied the Chair at the Semi-Centennial meeting, reviewed "some of the work which has been accomplished during the last half-century by way of a more accurate comprehension of the etiology, pathology and treatment of diseases of women by our American profession." He said, "The administration of glandular extracts after the removal of uterine appendages and in conditions demanding nutritive tonics, is attracting much attention and [they] are considered by many who have used them to possess much value."

Joseph Price, who spoke of unjust and great opposition to new ideas and techniques, said, "The young school of gynecologists have unfortunately lost interest or neglected plastic surgery." Wider use of pessaries and rest treatment for displacements were advised. He warned, "Be not deterred by false sentiment or the jealousies of those who would rather keep their patients in their own hands than see them cured by others from doing what we know to be our duty." He condemned the current methods of teaching, saying, "the student should be given that which will enable him, when he goes home, to go to work and do good work."

A. H. Cordier praised the A. M. A. meetings, his predecessors and the work of the past. He stressed need for early diagnosis and referred to use of "streptoserum" and "ointment of silver" in puerperal infections.

1900 to 1910

At the beginning of the 20th century, W. E. B. Davis praised asepsis and stressed the need for the use of rubber gloves. He elaborated on the truthfulness of the quotation: "Obstetrics married surgery and the fruit of their union was bright eyed gynecology." He condemned general surgeons for doing gynecologic and obstetric surgery and praised various specialty organizations and their journals. The place of myomectomies was recognized, but hysterectomy was generally considered to be better. He paid honor to Kelly but did not agree with his treatment of "pus in the kidneys through the ureter." The fact that the New York State Medical Society was not then in affiliation with the Association was bemoaned.

Henry P. Newman briefly traced the history of anesthesia by lumbar puncture and recognized it as an anesthetic method but said that the psychic trauma to women "consciously undergoing major operations upon their own viscera and witnessing details of its occurrence" detracted from its usefulness. He thought it was unreliable in obstetrics. His discussion included "Protozoon of Cancer"; "Removal of Lymphatics," in which he referred to Wertheim; "Ovarian Transplantation"; Vinot's work on "Tubal Epithelium"; and "Permeability of the Amnion." The following quotations are from his address: "Nothing could be more disastrous to the worth and dignity of this specialty, which has occupied for so long so honorable a place in medicine, than to allow itself to be considered and spoken of as one of the surgical specialties." "We are but just arriving at the threshold of the greatest era in our history, in which the full value of prophylaxis is being recognized, and gynecological knowledge and experience are to be the re-creator and conservator of health in women." "There will always be need for intelligent obstetrics while intelligent gynecology should eliminate itself at last by eliminating those conditions which are the cause of disease in women and its only excuse for being. Nothing but gynecology can eliminate gynecology."

J. H. Carstens spoke on "What of the Future?" He said:

> . . . Most questions in the obstetric part of our Section have virtually been settled and those in gynecology are being rapidly settled. Very soon there will be nothing to write about. . . . We should insist that gymnastics and systematic physical exercise should be taught in every school of the land, from the lower to the highest, and that the curriculum of study should embrace the most systematic course of gymnastics to produce a sound body with a sound mind. We should thoroughly study the effects and the results of erotism on the human body. We should study how we can more thoroughly bring about a more perfect marriage relationship and prevent the frequent mismating as shown in our courts. . . . In fact we must more thoroughly study the exact positions of individuals, every combination of physical and mental condition, and their most fit place and proper vocation in life. We must branch out, we must look ahead, we must be counsellors and the guides of the race in the future.

In discussing "The Trend of Gynecologic Work To-day," A. Palmer Dudley said, ". . . with the advent of Lister the Mephistopheles of surgery vanished from view. Fear no longer haunted the mind of operator or patient, and the peritoneum, the bugbear of former years, seemed to readily acquiesce in the evolution. With this confidence in the restorative powers of human nature came the reckless disregard of the consequences in the future." He stated that in 1887 he began "a series of experimental operations on the uterine appendages, which, strictly speaking, was more radical than a hysterectomy, because it trusted such surgical work on the appendages to the efforts of nature for a cure, while the ultimate results were more conservative to the woman, because by the skill of the surgeon and the aid of nature she had been restored to health, and could still consider herself a woman." Due credit was given to Carl Schroeder (1885) as being the pioneer. He said, "In doing conservative surgery on the tubes and ovaries the first thing to do is to endeavor to put the inside of the uterus into a condition to become healthy. If plastic work on the genital canal is necessary, this must be done also. Then open the abdomen and do what work is indicated in each individual case." He classified ventrofixation as a pernicious procedure differing markedly from suspension, the postoperative care of which he narrated.

L. H. Dunning included in "Remarks on Advances in Gynecology During the Last Year" the statement that treatment must be based on ideas of etiology and pathology; consequently, more work was warranted in those fields. He praised the work of Jenner, Pasteur, Koch, Lister, and Tate in discovering many sources of infection and said, "The moral is, let each man find an unsolved problem within the scope of his attainments, and then set himself deliberately and persistently to the task of its solution." He presented an excellent discourse on senile endometritis, and one of his photomicrographs was in color.

C. L. Bonifield commented that the office of the Secretary should be comparatively permanent and that the latter should be relieved of the necessity of disposing of bound volumes of the transactions and should be remunerated for his expenses. He suggested that the number of papers to be read be limited to 30, with only 15 minutes for each paper, and that the longer papers be read in abstract. He recommended changing the name to Section on Obstetrics, Diseases of Women and Abdominal Surgery, with 10 papers allotted to each branch. In discussing "Important Subjects Which Have Occupied the Attention of Gynecologists and Obstetricians During the Past Year," he included surgical and nonsurgical treatment of displacements of the uterus; surgery for cancer, stating that extensiveness of the operation depends on many factors; toxemia of pregnancy, recommending Veratrum viride; and vaginal cesarean section, advised in suitable cases. He also recommended that more work be done on sterility.

"The Legal Responsibility of the Physician for the Unborn Child" was the title used by C. S. Bacon. All physicians were advised to understand their lawful rights and obligations and to have a definite understanding or contract with patients. The fact that the unborn child must be regarded as another human being was emphasized. Consultations were advocated. He said, "In general it might be affirmed that the indications for destructive operations are becoming contracted and many pathologic states that previously were treated by embryotomy, would not now be accepted as indications."

J. Wesley Bovée directed attention to "The Status of the Fight Against Cancer." He discussed occurrence, classification, etiology, and treatment. Among his conclusions were that women should be educated as to signs and symptoms; there should be special care in classification; x-rays and radium are of little use in early cases, in which surgery is best;

radical surgery affords the best results; animal experimentation is promiseful; the vaginal route is not best for total irradiation; there are reasons to believe the disease can be controlled; and cancer should be regarded as contagious.

Walter B. Dorsett's lengthy address on "Criminal Abortion in Its Broadest Sense" was discussed by many participants. He advocated the obligatory teaching of medical jurisprudence and medical ethics in medical colleges, the enactment of good and sufficient laws and the amendment of insufficient laws now on statute books, and the appointment by the A. M. A. President of a Committee on Criminal Abortion for the purpose of attaining better laws through appointed state committees to work with their respective legislatures.

"Mental Alienation in Women and Abdominopelvic Disease" was W. P. Manton's subject. He said, "I and others have demonstrated that relief from suffering brings about a mental palliation often otherwise unobtainable." He believed that mental disease often stemmed from pelvic disorders but noted that it could occur without underlying physical pathology and that operative repair or restoration of the pelvic picture to normal was not always followed by a cure of the mental picture.

John G. Clark's "The Surgical Consideration of Congenital and Developmental Defects Leading to Obstinate Constipation" was so lengthy that a part was deleted prior to publication in The Journal. He recommended diagnosis by detailed clinical history and skiagraph. His admonition was that this kind of surgery is not for the novice.

1911 to 1920

1911 brought a change in title to Section on Obstetrics and Gynecology, and H. G. Wetherill spoke on "Retrospection and Introspection: Our Opportunities and Obligations." The closing paragraph was, "The crystallization and concentration of ideas, the simplification of practice, and the determination of what not to do, that we have done before, is progress of the best sort. Though this may not be our banner constructive period, it will be none the less valuable to humanity if we learn to see our mistakes of the past and to avoid them in the future."

The following year, under the chairmanship of C. Jeff Miller, "and Abdominal Surgery" was added to the name of the Section. In his dissertation on "The Present Status of Ligation or Excision of the Pelvic Veins in the Treatment of Septic Thrombophlebitis of Puerperal Origin" he said:

> The task of formulating the indications for the surgical treatment of puerperal infection still affords a source of prolific discussion. It seems impossible to agree on established rules as has been done in suppurative appendicitis, gall-bladder infection, or suppurative otitis media. Some of the confusion has undoubtedly arisen from the fact that we have no reliable clinical or laboratory guide to aid us in determining a reasonable prognosis, from the difficulty of differentiating the complex lesions, and to a certain extent, from the antipathy for serious surgical operations on the lying-in woman. It must be said, however, that our ideas are gradually crystallizing, that conservatism prevails, and that, owing to a better conception of puerperal processes in general, surgical measures adopted with more care and discrimination. During the past ten years the possibility of saving by operation the lives of women suffering from puerperal pyemia has received a great deal of attention. The idea is by no means new, as John Hunter suggested it, and scattered reports of successful ligation of the veins of the extremities can be found in the literature of the middle of the past century. The meager material at our command, reported by numerous operators, who have operated without definite indications and without a definitely established technic is sufficient to show that the procedure is feasible and should be given a fair and unbiased trial in septic thrombophlebitis.

1913 brought the birth of the American College of Surgeons, about the formation of which F. F. Simpson stated, ". . . it marks the beginning of a new era in American surgery. Its essential purpose is to encourage the development of sound surgical judgment to render surgeons more skilful and to make surgery more safe. It is not to be an exclusive, but an inclusive organization. It hopes to number among its fellows every one who does safe, sound and honest work." His lengthy address was on "Right-Sided Hypertension with Occasional Cardiac Dilatation as Postoperative Complications." At that meeting W. Wayne Babcock read a meritorious paper on "Spinal Anesthesia in Gynecology, Obstetrics and Abdominal Surgery."

E. Gustav Zinke's title was "A Few Points of Practical Importance in Obstetrics, Gynecology and Abdominal Surgery." He included discussion of "Intestinal Stasis," "Painless Operations," "Roentgen-Ray Therapy" (stating that although good results were obtained on fibroids, surgery was the treatment of choice), "Curative Effect of Radium," "Percy Treatment of Inoperable Carcinoma Uteri," "The Compromise Operations of Obstetrics," "The Treatment of Placenta Praevia" (advising case individualization); and "The Merits of Surgery in the Management of Puerperal Eclampsia," in which he reprimanded a writer who had recently stated the mortality rates were equal in hysterotomy or medical management. He favored use of such agents as Veratrum veride.

Thomas S. Cullen gave a panoramic view of "The Relation of Obstetrics, Gynecology and Abdominal Surgery to the Public Welfare" as he saw them 25 years prior and compared them to those of 1915. In his conclusions are the following statements: "Obstetrics must be made more attractive so that those entering this branch will not be tempted to leave it for less laborious fields." "Any Surgeon opening an abdomen should be capable of doing everything necessary in that abdomen. In other words gynecology and abdominal surgery logically belong together."

Edward Reynolds' scientific address on "Fertility and Sterility, Histologic Study of Spermatozoa, the Ovaries, and the Uterine and Vaginal Secretions in Their Relation to This Question," was well illustrated with photomicrographs.

Howard W. Longyear's discourse on "The Relations of Gynecology to General Surgery, Past and Present" emphasized that gynecology belonged to general surgery. He said:

> The Twentieth Century is ushering in a period of kaleidoscopic changes, of Aladdin-like transformations in everything pertaining to the activities of man. Science, the arts, business, society, finance, methods of warfare—all are feeling the jolts of the erratic and rapid pace of this great evolutionary present-day thrust. We are living in a new world in which habits and customs, venerated by centuries of usage, are dropped without ceremony and without apparent effort or regret, and the new blithely taken on, all in the name of progress. The horse bids fair soon to become extinct as a domestic animal, perhaps to revert to the wild state of his ancestors and be captured and exhibited by future generations of man as a curiosity, along with the gnu, zebra and giraffe.

Brooke M. Anspach's discussion of "Enterostomy and Enterocolostomy in the Treatment of Acute Intestinal Obstruction Following Pelvic Operations" concerned prevention, causes, stages, source of toxemia, and operative measures. He reported five cases illustrated with diagrams.

Thomas J. Watkins referred to the 70th A. M. A. Convention as the "Victory Meeting." He declared, "Democracy has defeated Autocracy." His subject was "Progress in Obstetrics, Gynecology and Abdominal Surgery." He said, "Study of the ductless glands has elucidated much hitherto obscure symptomatology of gynecologic cases, and has opened up a fertile field for further investigation. Radium has proved to be a remedy of great value. Much has been said relative to the practice of surgery by men with insufficient training. It it not my purpose or intent to offer any excuses for them, but to call attention to the fact that some of the responsibility for poor surgery rests elsewhere, especially with the men accountable to medical institutions of learning."

Reuben Peterson emphasized in his address on "The Future of Obstetrics and Gynecology as a Specialty" that they be combined. He condemned the tendency for gynecology to be linked with general surgery but stated that obstetricians and gynecologists must be able and prepared to cope with general surgical problems when they open the abdomen for pelvic disease. "Actual experience and technical skill in abdominal as contrasted with obstetric and gynecologic surgery should be acquired in departmental hospital clinics by cooperation with the general surgical clinics. . . . In fact, this principle of free interchange of services should not be confined to surgery alone, but should apply to all departments of the hospital, where such an arrangement will make for better training in obstetrics and gynecology."

1921 to 1929

John Osborn Polak discussed "The Defects in Our Obstetric Teaching." He recognized the decrease in many conditions "to an almost irreducible minimum" but stated, "Contrast this with the fact that the number of women who die from childbirth is increasing from year to year and that puerperal septicemia seems to be the only form of wound infection the occurrence of which has remained wholly unaffected in the past decade by the advancement of scientific knowledge." He praised classroom instruction but condemned lack of clinical observation in medical schools. "I feel that it is time that the public be taken into our confidence and taught what can be done by prenatal care and clean obstetrics; for good obstetrics would go far toward removing the horrors of childbirth and the consequent dread of invalidism. More than 61 per cent of all gynecologic surgery is the direct result of poor obstetric practice."

"Some Gynecologic Misdemeanors," a paper by Sidney A. Chalfant, contains the statement, "It is far from my intention to give the impression that my criticisms apply to the profession as a whole. There is no finer class of men, or men more conscientious, devoted, and skilful than the medical profession of America." For correction of evils, he advised more careful selection of medical students, more systematic instruction of students in history of medicine, so that they will have the inspiration derived from achievements of the past and receive inspiration for their own work; sufficient and efficient postgraduate schools for training the ambitious; and education of the public as to the necessity of obtaining competent surgical advice.

In his address "Abdominal Surgery Without Detached Pads and Sponges," Harry S. Crossen said, "A sponge left in the peritoneal cavity following an operation constitutes one of the most deplorable accidents of abdominal surgery." He mentioned the increasing number of lawsuits. His method, by which removal of gauze is automatic, was described by narration and eight figures.

Under the title "The Specialty of Gynecology," Frank W. Lynch reviewed the status quo, prognosticated, and outlined a plan of proper training in the future. He stated that gynecology was first to react to surgical possibilities and related how it developed along surgical lines. In his opinion obstetrics needed "a more conservative companion than general surgery." He emphasized the need of well-developed departments in medical schools in which obstetrics and gynecology are taught as interdigitating parts of one major division under control of one head. Close correlation between the clinic, ward, laboratory, operating and delivery rooms, and follow-up studies were recommended.

In the *Transactions of the Section* we find that the 1925 meeting was called to order by Vice-chairman H. C. Bailey. Apparently Chairman Rudolph W. Holmes was absent. The program included papers on tuberculosis of the vagina; distribution of the ovarian follicular hormone in human genital tissues; the average sex life of American women and the relation between experiences and genital findings; dilatation of the ureter and kidney pelvis during pregnancy; radium treatment of carcinoma of the cervix uteri: results at the Woman's Hospital, New York, after five years; the surgical treatment of varicose veins of the female pelvis; intracranial hemorrhages in the newborn; pelvimetry of the superior strait by means of the roentgen ray; and the treatment of hyperemesis gravidarum by intravenous injections of glucose and carbohydrate feedings.

George Gray Ward in his presentation, "Our Obstetric and Gynecologic Responsibilities," said, "This specialty comprises the study of the physiology and pathology of the reproductive system of woman, and as such should be considered in toto. There is a great need of propaganda to awaken the profession to the fact that obstetrics, as generally practiced at the present, is woefully below the standard that maternity hospital statistics show." He pointed out that septicemia, toxemia, and hemorrhage are responsible for 58% of deaths and are preventable. Condemning practice of bad obstetrics, he stated, "He who attempts to make nature deviate from her normal physiologic processes must remember that, while he may accomplish his immediate object, it is very apt to be at an exorbitant price. Patience is the better obstetrician, in the majority of cases, than dexterity." He emphasized the need of better teaching and training. A classification of wound healing was given. In conclusion he stated:

> I have said that our present shortcomings in obstetric practice must be due to inadequate teaching or a lack of conscience. . . . As to the second cause of our delinquency, what we need today is an awakening of our surgical conscience. Longyear has reminded us that skilful surgeons may not all be conscientious, and conscientious surgeons may not all be skilful. A full appreciation of this can best be brought to our attention by a proper audit of our results. To awaken our conscience, we must be made to appreciate the existing facts by bringing them out into the spotlight—to this end there is no answer but the word "audit." We must audit the morbidity statistics as well as the mortality statistics of our clinics as systematically and accurately as we do our finances —then only shall we see the light that will stimulate us to live up to our obstetric and gynecologic responsibilities.

Discussing "Indications for Surgical Intervention in Pelvic Lesions of Infectious Origin: Based on Seventeen Years of Laboratory and Clinical Study," Arthur H. Curtis included special features of vaginal discharges, endocervicitis, endometritis, and inflammation of the adnexa. He cautioned about operating for sterility alone and mentioned that for years he had tested tubal patency from within the abdomen with air. Conservative surgery was advised, and it was stated that at the time of operation the decision relative to disposition of the ovary required consideration of etiology of pelvic infection and that even though a hysterectomy was indicated the ovaries of young women should be left in situ unless one was dealing with tuberculous or streptococcic infection. He said that operative intervention should be avoided in patients with acute tubal inflammation.

Jennings C. Litzenberg spoke on "Obstetrics and Gynecology in Public Health Program," stating, "Enough facts and procedures are known to reduce the deaths of women by thousands every year if the profession would only apply the knowledge it already has. Why, in the name of humanity, it does not or will not is an enigma. There are enough lives lost which cannot be saved by anything known to medical science. May no more be added to these by neglect." In tabular form he showed the change in the death rate in the United States (1915-1925) as follows: Total puerperal deaths —2%, puerperal infection —11%, eclampsia +5%, cancer of female generative organs +12%, tuberculosis —40%, early infancy —20.5%, prematurity +10%, and birth injuries +14.8%.

Carl Henry Davis chose the subject "Obstetrics and Gynecology in General Practice." He commented on the development of anesthesia and analgesia in obstetric practice; devoted four paragraphs to the "Early History of the Section"; discussed "Maternal Mortality in the United States," saying, "puerperal sepsis still remains the greatest single cause"; and pointed out that "specialists in obstetrics and gynecology were almost unknown eighty years ago. While today there may be one or more in cities of 50,000 or larger, the care of women and children still remains a very important problem of the general practitioner." The need for more and better teaching of obstetrics was emphasized. He discussed "The Training of the General Practitioner" and summarized the conditions believed essential in the effort to obtain better medical care for women patients as follows:

> Governmental activities should be directed toward a careful survey of the causes of maternal and infant deaths in the United States and an investigation of methods that may be adaptable to various local conditions. Medical students who go into general practice after graduation require more adequate clinical training in obstetrics. More institutions are needed in which physicians who wish to specialize in obstetrics and gynecology may obtain the necessary training. There is a great need for graduate nurses who may qualify as midwives to work in conjunction with the medical pro-

fession in the care of a large group of women who are unable to pay for adequate obstetric service under existing conditions.

1930 to 1939

James C. Masson spoke on "The Trend of Present-day Medical Education," stating that it is toward scientific medicine and specialization, which is not altogether due to the desire on part of physicians but is a natural reaction to demand made by the public. He said:

> It is difficult to see a satisfactory solution of the problem of furnishing adequate medical care for all the people at a cost which they can pay, but in recent years investigations which may lead to a solution have been begun. We can await the outcome of these studies, which are in able hands. Our task, meanwhile, I think, should be to help general practitioners to acquire adequate experience in obstetrics and gynecology, and to provide for admittance to the rank of specialists in obstetrics and gynecology only those who at the same time have a sufficient basis in general medicine and sufficient expertness in one special branch to enable them to render adequate service.

In 1931, the Section's annual volume, *The Transactions of the Section on Obstetrics, Gynecology and Abdominal Surgery,* was discontinued. Speaking on "The Biologic Significance of the Female Reproductive Cycle," Emil Novak stated that gynecology's "early history is a record of brilliant achievement in the development of operative procedure, and a subsequent generation has added comparatively little to this branch of our work. . . . Pathology is still, and always will be, a sine qua non in the proper training of the gynecologist. During recent years the line of advance has again shifted, for certainly at the present time physiology must be recognized as the growing margin of our specialty." He acknowledged the help of the anatomists and physiologists. In his discussion of periodicity in the female sex functions we find: "Periodicity may be said to be the rule of the universe." He recorded "some of the accomplishments and some remaining problems" and concluded with "the female sex cycle as distinguished from the female reproductive cycle." His closing paragraph expressed dependence on our allies in the laboratory, and he quoted from one of his papers: "So long as we recognize this dependence, and so long as we are willing to follow the line of scientific march rather than cavort ahead of it, we may perhaps be pardoned for an occasional display of overenthusiasm. After all, the latter is usually due to the fact that we have human beings to cure, just as the laboratory worker has scientific problems to solve."

Fred L. Adair, first president of the American Committee on Maternal Welfare (1934) and first president of the National Federation of Obstetric-Gynecologic Societies (1945), spoke on "The Interrelationship of Mother and Fetus" at the 1932 meeting. Included in his statements were these: "The exact relative importance of heredity and environment is not known." "We know that certain toxins will destroy germ cells. In all probability, they are subject to injurious influences which may not destroy their potency but which lead to subtle changes." He discussed "The Critical Early Period of Pregnancy," "Hormones," "Pathologic Conditions," and "Other Changes." His concluding sentence was, "These relationships are affected by the heredity of the parents, by the growth and development of the potential mother, by the character of the germ cells, by the maternal environment throughout pregnancy, by the critical period of parturition and, to a lesser degree, during the postpartum and postnatal periods."

Barton Cooke Hirst discussed "The Four Major Problems in Gynecology." He thought that "one of every eight women who reach the age of 35 will have cancer" and stated that there should be provision for both surgical and radium treatment. Concerning maternal mortality he said, ". . . half of these deaths are preventable." He considered "sterility" and "birth control." His address was somewhat philosophical and was terminated as follows: "In attempting to review so much in so short a time, I am aware that I give only the merest hints that may, perhaps, invite others to more productive thought, especially the younger members of the profession. We may confidently leave to them the problems vexing us. It is certain they will reach for higher levels of achievement than we have attained."

Joseph B. DeLee in his "Obstetrics Versus Midwifery" stated that contrary to the dictionaries he did not consider these terms synonymous; "midwifery is the practice of midwives, male or female, and obstetrics is the practice of the scientifically trained physician." He traced the historical development of midwifery and pointed out:

> . . . Until very recently the practice of normal obstetrics by physicians has been looked down on by the profession and by the public as well as by the midwives. . . . The public in many places still believes that his [the obstetrician's] accomplishments are less than those of the medical men and the surgeon. The medical schools, in many universities, still rate obstetrics as a minor specialty. . . . Hospitals do not provide equal facilities for obstetrics as for surgery. . . . All my medical life I have striven to eradicate this low opinion of obstetrics and to place on equally high pedestals the three primary branches of medicine, obstetrics, medicine and surgery, all equally important, all equally dignified.

He discussed "Disturbances of Pregnancy," "Labor," "A Natural Delivery," and "Attainment Through Education," bemoaning the fact that there were insufficient schools, teachers, material, and support. He believed in teaching the beauties of normal obstetrics, asepsis, intelligent expectancy, and trusting in nature.

James R. McCord, who was to be the first president of the South Atlantic Association of Obstetricians and Gynecologists three years later, was the 1935 Chairman. His presentation on "Syphilis and Pregnancy: A Clinical Study of 2,150 Cases," contained many statistical studies. His conclusions were as follows:

> 1. Pregnancy does not affect the reliability of the Wassermann reaction. 2. This test should be a routine part of antepartum care. 3. Regardless of the activity of the disease, sufficient antepartum antisyphilitic treatment assures the woman a syphilis-free baby in 95 per cent of the cases. 4. The best results will be obtained with ten or more treatments. 5. Treatment should be mild but continuous and should not be controlled by the Wassermann reaction. 6. The concurrent use of arsenic and a heavy metal has worked well in our hands. 7. Such therapy seems to be safe for the mother. 8. In the vast majority of cases, a strongly positive cord Wassermann test, properly done, means that the baby has congenital syphilis. A negative cord Wassermann reaction is of little value in the diagnosis of congenital syphilis. 9. The characteristic picture of osteochondritis of the long bones is pathognomonic of congenital syphilis. 10. There seems to be no condition in medicine that returns such huge dividends in life and health with such a small output of energy and money as that seen in the prevention of congenital syphilis.

In "Trends in American Obstetrics During the First Third of the Century," by Lyle G. McNeile, we find the opening sentence: "Although many notable advances and changes have been made in the practice of general medicine and surgery during the present century, in no specialty have there been more drastic changes than in obstetrics." He pointed out: ". . . at the beginning of this century every general practitioner had perforce to be an obstetrician; but at this time the new fledged doctor obtained his diploma to practice with little or no actual experience in clinical obstetrics. There were at this time not more than a half dozen medical schools that maintained lying-in hospitals in which medical students could witness deliveries, and the student who had actually delivered one or two women before he was graduated was considered very lucky." He discussed "The Dawn of New Obstetrics," "Causes That Contributed to the Changed Tendencies in Obstetrics," "Trends of the New Obstetrics," "Obstetric Education," "Is Pregnancy a Disease of Nine Months' Duration?," "Trend Toward Making Obstetrics Easier for Patient and Physician," "The Elimination of the Midwife," and "Apparent Trends Characterizing Obstetrics in Present Century."

Pierce Rucker discussed "The Treatment of Eclampsia," dividing it into two parts: preventive and curative. He strongly emphasized the former, stating that it should start when there is a rise in blood pressure or unusual gain in weight. Statistics on 129 treated cases were related under the headings "stopping the convulsions," "good nursing care," "promoting kidney function," and "digitalis," of which adequate dosage was deemed mandatory.

The Section on Obstetrics and Gynecology was the title used beginning in 1938. In "The Undergraduate Teaching of Obstetrics," E. D. Plass discussed factors relating to the problem and offered "a considerable defense of the men now actually engaged in obstetric teaching." It was pointed out that modern obstetrics is actually a field of preventive medicine. Didactic obstetric teaching was rated par with instruction in the other medical clinical branches, but it was emphasized that the clinical instruction could not be expected to result in competency to handle all obstetric emergencies. He pled for the more effective utilization of the trained and experienced obstetric specialists but appreciated the fact that changes in medical thought would inevitably be involved, requiring time.

Harvey B. Matthews directed attention to "Obstetric Shock: Its Causes, Recognition and Management." An historical account is given. The primary principles were elaborated. His concluding statement was as follows: "Real progress in the prevention, recognition and management of shock lies not only in cultivating the art of obstetrics but in the study of biologic principles that concern reproduction, function, nutrition, metabolism and the repair of tissues, and in the thoughtful application of this knowledge. With the mastery of these principles clinical experience and the maturity of years will give that degree of sound judgment which every physician doing obstetrics—general practitioner or specialist—longs to attain."

1940 to 1949

The 1940 address of Ludwig A. Emge, "Present Trends of Socialization of Medicine in Relation to Maternal Welfare," exemplifies intelligence and foresight, as time has proved. In a discussion of the aim of socialization, the national health program, the care of migratory workers in California, hospitalization, and the position of physicians in administration, the plea is made for enlightenment of the profession, the development of sound convictions, and "action—organization and cooperation —and this must come from within our ranks."

The following year Norman F. Miller discussed "The Perpetuation of Error in Obstetrics and Gynecology," listing the circumstances which "combine to make our time particularly susceptible in this respect" as the World War; "endocrinology, the beautiful romantic young maiden of modern medicine, who keeps us dizzy with her therapeutically provocative gyrations;" overzealousness in the field of medical writing; and blind adherence to obsolete ideas in our specialty. Careful consideration was given to "Errors That Are Being Perpetuated," "Perpetuation of Obsolete Standards," and "What to Do About It." He closed with this sentence: "If we recognize our responsibility and accept this challenge, if we are unafraid and willing to think and plan in terms of a newer and better standard of medical care for the pregnant woman, then I foresee for obstetrics, for maternal and child health, a new and great future."

The 1942 address, "The Educational Objectives of the American Board of Obstetrics and Gynecology," presented by Walter T. Dannreuther, president of the board since its founding 12 years prior, deserves to be read in its entirety.

The 1943 meeting was scheduled for San Francisco, but, because of war, only the Board of Trustees, Executive Committee, and the House of Delegates met. The next year, Louis E. Phaneuf's "The Changes in Operative Gynecology During the Last Quarter-Century" was summarized as follows:

> The last quarter of a century has shown significant improvement in surgical technic, with emphasis on careful dissection and ligation of individual vessels with fine material rather than mass ligature of tissues. The treatment of carcinoma of the cervix has changed from surgery to irradiation with the return to the radical pelvic operation by a few gynecologists in early cases and good surgical risks. Carcinoma of the uterine corpus and fundus has remained a surgical lesion, surgery, however, having been complemented by irradiation. Improvement in the operation of myomectomy has resulted in more conservative management of these lesions in the young; supravaginal hysterectomy still remains the common method in use, while an increasing number of gynecologists have turned to panhysterectomy as a prophylactic means against carcinoma of the cervical stump. Vaginal hysterectomy has been reborn and improved and has now become a commonplace procedure. The increased number of surgical vesicovaginal fistulas has been responsible for the elaboration of new technics in the cure of this lesion.
>
> Trachelorrhaphy and amputation of the cervix are less frequently done, these having been replaced in many cases by cauterization and electrocoagulation. A significant advance has been made in the surgical treatment of uterine prolapse, cystocele, and rectocele through better anatomic understanding of these lesions and by reconstructing the deficient supports through the vagina rather than by depending on abdominal suspension or fixation of the uterus. Pelvic inflammatory disease has been handled more and more by conservative methods, and the sulfonamide drugs seem to show great promise in lessening and eradicating this condition. Ovarian tumors have been better classified, the rare tumors have been discovered, the tendency of malignant changes in these neoplasms has been emphasized and their early ablation has been strongly advised.

The 1945 meeting was canceled due to war, and only the Board of Trustees, Executive Committee, and House of Delegates met. The next year, Philip F. Williams, to whom should go the highest of praise for his efforts in bringing into existence in 1951 the "national organization for ethical, competent obstetricians and gynecologists," spoke on "Maternal Welfare and the Negro." The reprint distribution of this address was considerable. His closing paragraph was as follows: "Obstetric care has undergone an evolution in this generation, but the Negro has not participated fully in the benefits of modern obstetrics. It is not possible to have two systems of maternal welfare; there must be one all-inclusive health program. Health education and adequate maternity care for the Negro are amply provided for in the proposed national health program of the American Medical Association. Conservation of human life in the process of reproduction should be shared equally by all Americans. The interest and activity of the medical profession can bring this about."

Alice F. Maxwell was in the Chair at the A. M. A. Centennial session of the Section. Her subject was "A Medical Inventory." Unfortunately, this address evidently was not published and a copy of the manuscript is not available.

William F. Mengert's "Estimation of Pelvic Capacity" included the listing of the five components of cephalopelvic disproportion as "size and shape of bony pelvis, size of fetal head, force exerted by the uterus, moldability of the head, and presentation and position." His discussion of subjects, methods, interpretation, and results and his comments are excellent and should be read in full.

1950 to 1957

"Reproduction in the Older Woman" was the title of the address by L. A. Calkins, and it included 10 tables of interesting data. In his summary and conclusions he stated:

> Older pregnant women, like other women of the same age but not pregnant, are more apt to have fibroids, hypertensive cardiovascular disease and, perhaps, carcinoma than are younger women. They are, therefore, deserving of the most careful and complete examination of all their organs and functions. The analysis also seemed to show that labor and the results thereof, except for a possible extremely moderate increase in fetal mortality, can be expected to progress along the same lines as for the younger groups. Our present fear of the outcome of pregnancy for the elderly primigravida is no more justified than would be such a fear for the elderly multigravida.

James Ramsdell Bloss, Chairman of the A. M. A. Board of Trustees in 1944, discussed "Causes of Fear Among Obstetric Patients" in his 1950 address, emphasizing that obstetricians and gynecologists must understand and "practice the humanities as well as the science of the medical profession." He included discussion of "Fears with Psychologic Basis," "Basic Conflicts," and "Fears with Legitimate Basis." It was pointed out that there has been too much disturbing publicity about the Rh factor. Frank, encouraging discussions with patients in the light of scientific medical accomplishments were recommended.

"The Test of Labor–An Evaluation of Its Present Worth," by Arthur B. Hunt, contained 10 tables. His conclusions were well drawn. They included this statement: ". . . to date there is no better way to justify an initial cesarean section than a failed test of labor." It also tests the obstetrician's "powers of observation, vigilance, judgment, obstetric conscience, and technical skill."

Louis H. Douglass spoke on "Repair of Obstetric Soft Tissue Damage Immediately Post Partum," based on an experience of about 17 years of practice, under the headings of "Cervical Repair at Delivery," "Perineorrhaphy at Delivery," and "Advantages of Elective Perineorrhaphy." He had been pleased with his anatomic results, and the expressions of gratitude from patients had been very rewarding.

Albert W. Holman was elected to the chairmanship for the 1953 meeting, but he died in 1952, being succeeded by Vice-chairman R. Gordon Douglas.

"The Challenge of Dystocia" was the subject of Chairman Bernard J. Hanley. His second paragraph began, "Prolonged labor per se is not necessarily harmful, but prolonged labor accompanied by a difficult forceps operation is a combination that always causes injury to the mother and is frequently lethal to the baby." He emphasized that patients in prolonged labor should be properly sedated and given adequate fluids. He and his co-workers had obtained excellent results in determination of the anterior pelvic depth by the use of the Hanley-McDermott pelvimeter, which he considered a rational procedure for determining the possibility of midpelvic or outlet dystocia.

Frederick H. Falls spoke on "Conquest of Eclampsia." A résumé of this is as follows:

> The convulsive stage of eclamptogenic toxemia has been gradually eliminated in three hospitals over a period of 20 years, despite the fact that eclampsia remains one of the three most common causes of maternal mortality in the country as a whole. The improvement is related to the increasing frequency with which toxemia is recognized and the systematic attention given to it. The mild nonconvulsive forms of toxemia, found and treated early, are without much danger. It is the convulsive stage of the disease that does irreversible or fatal damage. A simple program of management that has been developed must be brought to bear as soon as toxic symptoms appear and must be continued until the symptoms are brought under control or the patient is delivered. The program includes strict prenatal care, hospitalization if ambulatory care proves insufficient, induction of labor if the toxemia progresses, and cesarean section if certain indications exist. Although more knowledge of this disease is needed, the means for preventing most of the deaths that now occur are already available.

In 1956 Frank R. Lock discussed "A Concept of Operative Gynecology," which he summarized as follows:

> Operative gynecology is a major field of medical practice. Although the pathological significance and natural history of pelvic lesions is well known, the methods of management by the profession at large are variable. The arbitrary application of surgical procedures, according to the basic principles of the removal of pathology or correction of anatomical defects, is not acceptable in the field of gynecology. The effects of a given operative procedure must be weighed against the consequences of other management of existing pelvic pathology. It is possible to establish beyond a reasonable doubt that relief of symptoms will result from operative or nonoperative treatment in gynecology, through exact diagnosis and appraisal of the related pathologic, physiologic, and psychologic processes of women.

In 1957 D. Frank Kaltreider gave an address on "Fetopelvic Grading of Breech Presentations." THE JOURNAL's summary follows:

> In the management of a breech presentation, three factors must be considered in order to decide between vaginal delivery and cesarean section. These are (1) pelvic size, (2) pelvic shape, and (3) estimated fetal weight. Pelvic size can be accurately measured by x-ray pelvimetry. Unless the infant is premature, vaginal delivery is contraindicated in flat pelves with an obstetric conjugate of less than 10 cm. Fetal weight is best estimated by having four or more examiners give an estimate without the knowledge of others and averaging the estimates. In addition to the above three factors, the behavior of the sacrum and consideration of uterine inertia must also be taken into account.

Comment

Conceived by its 12-year-old mother, the A. M. A., the Section was born at term in 1860, being given the name "The Section on Practical Medicine and Obstetrics." That appellation was subsequently changed as follows: 1867, Section on Practice of Medicine and Obstetrics; 1873, Section on Obstetrics and Diseases of Women and Children; 1880, Section on Obstetrics and Diseases of Women; 1911, Section on Obstetrics and Gynecology; 1912, Section on Obstetrics, Gynecology and Abdominal Surgery; and 1938, Section on Obstetrics and Gynecology. Prior to 1958, the Section had held 93 meetings in a total of 30 cities, including Atlantic City, N. J., Chicago, and San Francisco, ranking in that order of frequency. War caused cancellation of the 1861, 1862, 1863, 1943, and 1945 meetings. The life of the Section has at times been impassioned and troubled, as exemplified by the Civil War years and the proposal of an abolition amendment in 1888. It has had its hours of bitterness and its reports of tragedy, but these are greatly outweighed by its superb and glorious hours. Mindful of its accomplishments and thankful to the Great Physician for them, we look to the future with anticipation of continued progress and happiness.

4240 Magnolia St. at General Pershing (15).

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ANTICOAGULANTS—A COOPERATIVE EFFORT

THE advent of heparin and bishydroxycoumarin (Dicumarol) in the late 1930's and early 1940's as useful drugs for the management of thromboembolic disorders started a chain of events that went far beyond their use as agents for the treatment of thrombophlebitis. Anticoagulants have become generally accepted in the management of long-term and short-term therapy of coronary artery disease and myocardial infarction [1] and for the prevention or amelioration of certain cerebrovascular diseases.[2] Their availability has opened new areas of investigation into the mechanism of blood coagulation. Their promising use in cerebrovascular disease has occasioned a new and more precise classification of cerebrovascular diseases because, in the words of a committee of the Advisory Council for the National Institute of Neurological Diseases and Blindness, Public Health Service, the practitioner now has available powerful drugs which alter the coagulability of the blood. Hence diagnosis now becomes imperative not only as a means of directing therapy but also for further scientific study.[3] A premium is now placed on diagnosis of cerebrovascular disease, for the days of fruitless therapeutic maneuvers may be past.

Public interest in these drugs is reflected by the news concerning the President's use of an anticoagulant and more recently by the direction of the Senate Appropriations Committee to the National Institute of Health to study the action and utilization of anticoagulant drugs as aids in the treatment of coronary and cardiovascular disease (strokes). The directive was backed by a 2-million-dollar appropriation (Senate Report No. 17191, 85th Congress, 2nd Session, p. 28).

No less important has been the development of new coumarin compounds that made the use of anticoagulants more practical than bishydroxycoumarin, the first of the synthetic anticoagulants. Unfortunately, no useful substitute for natural heparin has appeared. Several recent reports in THE JOURNAL on warfarin sodium are examples of progress in that direction.[4] Interestingly enough both drugs had their origin in the same laboratory at the University of Wisconsin. Of equal interest is the fact that these valuable additions to the drug armamentarium came from unfettered research or as Link, the discoverer of bishydroxycoumarin and of warfarin, put it: "I think the secret of their success (his students) is three-pronged: they never ceased to wonder; they kept on trying, and they were on a project toward doing mankind some good instead of trying to destroy it." In these words, the aim of American medical research can be summed up.

Useful modalities in science and medicine do not come in full bloom. They develop by slow stages and from devoted workers. A review of the progress of the past 20 years in a symposium honoring the late Dr. Jay McLean by those intimately involved has recently appeared.[5]

Dr. Irving S. Wright, one of the most active proponents of anticoagulant therapy, pointed up the diseases susceptible to control by anticoagulants: "Today, throughout the civilized world and on both sides of the iron curtain,[6] anticoagulating drugs are used in a steadily increasing number of conditions. They are under study in hundreds of institutions. It is estimated that over one million persons suffer from thrombosis or embolism in the United States each year. These conditions include idiopathic, postoperative and traumatic thrombophlebitis, myocardial infarction, rheumatic heart disease with embolization, thromboembolism in pregnancy, peripheral arterial thrombosis and certain selected examples of cerebral thrombosis and embolism. More than four hundred thousand persons die each year with thrombosis or embolism as the terminal event. For each of these conditions and for many others, anticoagulant therapy has been used and should be considered. For some the indications are well established, for others the final chapters have not been written."

The four speakers, Drs. Irving S. Wright of the New York Hospital, Charles H. Best of Toronto, Canada, Armand T. Quick of Marquette University, Milwaukee, and Karl Paul Link, each presented his part in this story, which has since captured the interest of legislators.

Thanks to Dr. Wright, the reader can see the part played by the Association through its then Council on Pharmacy and Chemistry in the early days of bishydroxycoumarin. Several of his early patients developed hemorrhagic complications which had not been noted by those who worked with the compound earlier. He reported this incident and thus prevented the premature release of the drug until fully adequate studies permitted the development of safe directions for use. Through the action of the Council, many tragedies were averted by this cautious step. Indeed, this step may have averted the possible rejection of the coumarin anticoagulants in these early trying days. The reasons need not be detailed further than to point out that adequate methods for clinically controlling the reversible hypoprothrombinemia had not been fully developed. Fortunately, time and experience have placed the control of the reversible hypoprothrombinemia in proper perspective and on sound ground.

The method most commonly used to regulate dosage of bishydroxycoumarin and other anticoagulants which stemmed from it is the one-stage method, developed by Dr. Armand J. Quick. The test is taken for granted today, but the recital of the steps to reach this goal were retraced by its discoverer. Without the test or its modifications the availability of clinically useful anticoagulants would have been delayed. The use of a prothrombin determination cannot, as yet, be divorced from the administration of anticoagulants. Both complement each other. Just as the drugs themselves led to newer understanding of blood coagulation and the use of drugs which alter it, the newer methods such as prothrombin consumption time, the partial prothrombin test, and the thromboplastin generation tests are outgrowths of the one-stage prothrombin time test.

While the coumarin compounds are commonly associated with the term anticoagulant, the fact that the isolation of heparin and its use in thrombophlebitis antedated bishydroxycoumarin as an anticoagulant drug is often overlooked.

Modern heparin is due largely to the efforts of the late Dr. Jay McLean, who became interested in it as a student at Johns Hopkins University. In the very personal account of McLean's involvement with heparin, Dr. Charles H. Best of Toronto traced an item of purely physiological interest to therapeutics. This effort was truly international, for with the availability of purified heparin, Dr. Gordon Murray of Toronto made clinical trials in 1935, followed by Drs. Eric Jorpes and C. Craaford of Stockholm. The early finding that certain types of clinical thrombosis could be prevented by treatment with heparin has been amply confirmed.

It was early recognized that heparin, while an effective agent for prevention of clinical thrombosis, had serious disadvantages. The supply was limited by virtue of a limited supply of starting material, lung tissue; because it was active only on intravenous use, its action was short and consequently highly expensive.

The meeting of purely physiological and clinical studies came about originally through a veterinary and agricultural problem. Link, of Wisconsin, in 1933 started out to develop a strain of sweet clover which would not impart the hemorrhagic disease noted earlier in cattle who were fed on silage made from sweet clover. How the goal turned from cattle to man was told by Link. But bishydroxycoumarin was only the beginning of a large number of synthetic derivatives related to the parent compound, for as Link, the chemist, forecast in 1944, "we might be at the beginning of things and not at the end in this field of study."[7] The clinician, E. V. Allen, who was among the first to use bishydroxycoumarin clinically echoed in 1946 a similar sentiment: "Advantageous as both heparin and Dicumarol are, use of them represents only the first steps in the direction of securing satisfactory anticoagulants for clinical use."[8]

In the years intervening between the isolation and synthesis of bishydroxycoumarin, Dr. Link and his students set themselves another goal—to obtain an anticoagulant compound which would have "most of the desirable features that can be expected from an anticoagulant that can be given via the oral route." Earlier the clinicians virtually snatched a "cow-poison" for a human drug, but accepting a compound with a high rodenticidal value as a human drug was not so readily done. Fortunately, an aborted suicide attempt with a rodenticide containing warfarin paved the way. An article in THE JOURNAL[9] detailed the recovery of a patient after ingestion of large amounts of warfarin. In due time, the Wisconsin group provided water-soluble warfarin sodium for clinical use. The appearance of a score of papers on this compound since its introduction in 1954 led Link, the last of the quartet, to state: "It is my firm belief that in time it [warfarin sodium] will replace Dicumarol on the basis of its performance over a wide variety of conditions and that other anticoagulants of the Dicumarol type [including the many made in the Wisconsin laboratories] will not be superior." This view by one who has been responsible for the original impetus in this field represents a standard for future anticoagulant compounds. Whatever the future may bring in this respect, the physician who uses anticoagulants will want to keep in mind the triad of Link for successful use of anticoagulants. Successful anticoagulant management calls for (1) clinical judgment, (2) proper prothrombin determinations, and (3) the ready availability of vitamin K. The current literature on anticoagulants indicates that this is being heeded.

Thus the clock has made a full turn. The isolation of heparin by McLean and its purification by the Toronto group, the turn of a hemorrhagic disease of cattle to a human drug, the development of new methods to study blood-coagulation processes, the establishment of the value of anticoagulants in the treatment of myocardial infarction and a host of other thromboembolic conditions, the initiation of studies to assess their value in prevention and amelioration of strokes, and a new classification of cerebrovascular disease occasioned by these findings represent an excellent example of synthesis of laboratory and clinical developments going hand in hand.

Here is a historical account of unfettered research by free men at their best who set out to do some good instead of trying to destroy life. Here is a story of the intertwining of isolated effort; all the strands of which are playing a significant role in the present and future control of atherosclerotic and thromboembolic disease. Clinicians and laymen alike will watch with interest a forecast recently made: "If these trends are corroborated [reduction of morbidity in coronary artery disease], long term anticoagulation is the first distinct preventive agent in arteriosclerotic disease."[10]

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INCOME TAX GUIDE

Last year, on March 1, 1958, THE JOURNAL published a special edition entitled "1958 Federal Income Tax Guide for Physicians." Copies of this guide are still available on request to the A. M. A. Law Department, 535 N. Dearborn St., Chicago 10.

LONG DISTANCE TELEMETERING AND MONITORING

The development of lightweight radio equipment for artificial satellites to transmit back to the earth environmental information about space and planets may also assist physicians and physiologists to gather physiological data on human beings and animals while ambulant and with normal freedom of movement. The equipment need not be so rugged as to withstand the large accelerative forces of a rocket but can be sufficiently sturdy to resist damage of accidental falls and to function under the vigorous bodily movement of athletes and men and women at their regular work. The equipment could record data also on sedentary patients.

Miniature broadcasting equipment and its uses have been dealt with in an article by Beenken and Dunn.[1] They visualize transmitters of not more than 2 lb. (0.9 kg.) in weight that can be operated by persons without radio engineering experience and that are nondirectional, within the tolerance of Federal Communications Commission recommendations, and with battery life of at least 100 hours.

Beenken and Dunn mention a list of physiological functions that can be studied with reasonable accuracy, such as temperature, pulse pressure, exercising tests, and oxygen demand. The physician might study cardiac output potential and record electrocardiograms while his patients are working at their regular jobs, and he might observe physical and physiological effects on patient-executives at the conference table. In the event the transmitter is made smaller (and one has already been made small enough for a man to swallow), the physiological changes in athletes may be observed while they are participating in competitive sports. Undoubtedly much discussion will ensue if and when football coaches read meters of electronic instruments to determine whether a player is tired and at the point of exhaustion.

These are a few of the achievements to be realized in the near future by the cooperative efforts of physicians, physiologists, and engineers. Increased interest in medical electronics is exemplified further by such meetings as the Conference on Electrical Techniques in Medicine and Biology, held in Minneapolis after the recent A. M. A. Clinical Session, and the meeting in New York, March 23-26, of the Institute of Radio Engineers, which has scheduled papers dealing with the applications of electronic tools and instruments to physiological, diagnostic, and clinical procedures.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Nine months ago the Chairman of the A. M. A. Board of Trustees, Dr. Leonard Larson, pledged our Association to a dedicated and continuing effort to improve the health care of the aged. He made this vow in testimony before members of the House Ways and Means Committee in Washington, D. C.

Has the A. M. A. kept Doctor Larson's promise? Has medicine taken specific action at the national and state levels on the aged problem?

The answer is an emphatic yes. For example, the A. M. A. House of Delegates took farsighted action when it approved a proposal calling for development of an effective voluntary health insurance or prepayment program for the group of persons over 65 years of age with modest resources or low family income. Within three months official groups of several states—West Virginia, New Jersey, California, Texas, Ohio, Michigan, Florida, Iowa, and others—moved decisively on the A. M. A. policy recommendation. In addition, 34 state medical societies will give the matter top priority at their annual meetings this spring.

What are some of the states actually doing? In West Virginia the Association's Committee on Blue Shield has recommended that physicians accept 50% of their normal fees for Blue Shield clients over 65 years of age who have an income not exceeding $3,000 per annum. New Jersey has approved the A. M. A. policy and urged the Medical-Surgical Plan of New Jersey (Blue Shield) "to prepare a contract offering coverage at reduced premiums to people over 65 with reduced income."

Your A. M. A. also is working closely with commercial insurance organizations to encourage the development of new insurance programs and expansion of existing lower-cost protection.

Policies already available include some guaranteed renewable contracts, "paid-up-at-65" policies, senior security contracts, and "65-plus" policies. To further strengthen and improve private insurance coverage for those over 65 years of age, the Health Insurance Association of America has asked its 265 member companies to make available (1) policies guaranteed renewable for life, (2) coverage to persons now over 65 years of age, (3) coverages that will continue after retirement, and (4) the inclusion in the group contract of the right to convert to an individual contract at end of employment.

Through medical societies and the insurance industry sound and inexpensive protection to persons in the senior citizen bracket is being broadened and improved faster than many thought possible only a few months ago. We are not, however, confining our efforts to the development of financing mechanisms only. Solution of financial problems relating to the health care of the aged also depends on reductions in the costs of services.

Your A.M.A. believes that there is an undeniable need for new and improved facilities tailored to the specific health requirements of older citizens. Therefore, we vigorously support a government-insured loan program of the FHA type for nongovernmental hospitals and nursing homes whether their ownership is of a nonprofit or proprietary nature. We also recommend changes in the Hill-Burton act to make it possible for states to put more money into nonprofit nursing homes.

These then are some of the forward steps taken by your Association, the state medical societies, and the health insurance industry to improve the health care of the aged. No one can deny that there has been solid progress; we cannot deny that there is still much to be done. However, medicine and the members of the health team are in positive, forward motion against problems that not long ago may have seemed insurmountable.

GUNNAR GUNDERSEN, M.D.
La Crosse, Wis.

MEDICAL NEWS

ALASKA

Annual Meeting Held in Juneau.—The Alaska State Medical Association held its 14th annual meeting March 19-21 in Juneau under the presidency of Dr. William M. Whitehead. The guest speakers were Drs. Edward Morgan, clinical assistant professor of medicine, University of Washington Medical School, Seattle; Raymond F. Peterson, division of pathology, Murray Clinic, Butte, Mont.; and Robert A. Pommerening, clinical assistant professor of dermatology, University of Washington Medical School, Seattle. Addresses were given by Acting Governor Hugh J. Wade and Mr. M. L. MacSpadden, Mayor of Juneau. A panel discussion on "Ulcerative Colitis and Irritable Bowel Syndrome," held March 20, was moderated by Dr. Morgan. A film, "Surgical Repairs of Facial Lacerations for Optimum Cosmetic Results," and exhibits were held. The banquet, the evening of March 20, was held at the Baranof Hotel. A ladies' program was also arranged.

CALIFORNIA

Radiologist Given Award.—The Gold Medal of the American College of Radiology has been awarded to Dr. Robert S. Stone, chairman, department of radiology, University of California School of Medicine, San Francisco. The Gold Medal is presented annually "for distinguished contributions to radiological medicine." Dr. Stone joined the university faculty in 1928 and became professor of radiology in 1938. From 1942 to 1946 he was associate project director for health at the Chicago Metallurgical Laboratory of the atomic bomb project. After the war he developed and now directs the Radiological Laboratory at U. C. Medical Center, where physical, chemical, biological, and clinical investigations are conducted with the 70-million-volt synchrotron.

Name Dr. Kretchmer Department Head.—Dr. Norman Kretchmer, associate professor of pediatrics at Cornell University Medical College, New York City, and associate attending physician at New York Hospital, will succeed Dr. Robert H. Alway as head of Stanford University's pediatrics department, effective July 1. Dr. Ruth T. Gross, associate professor, has been acting head of pediatrics for the past two years. Dr. Kretchmer spoke in San Francisco Feb. 24 before the Northern California Chapter of the American Academy of Pediatrics. Last year the academy presented him with the E. Meade Johnson award for distinguished pediatric research. Dr. Kretchmer has taught at the University of Minnesota, Minneapolis, and the State University of New York.

COLORADO

Biography of Florence Sabin to Aid Research.—The University of Colorado Press, in connection with the state's Rush to the Rockies centennial observance, is publishing "Florence Sabin: Colorado Woman of the Century," a 222-page book, written by Mrs. Elinor Bluemel, of Englewood. The book traces the life of Dr. Florence R. Sabin, world-famous medical researcher, teacher, and humanitarian, who died in 1953. It contains eight pages of photographs. All royalties from the sale of the book will go to the University of Colorado School of Medicine for research in cellular biology. A statue of Dr. Sabin was dedicated Feb. 26 in Statuary Hall in Washington, D. C. She is the first Coloradan to receive such an honor. Born in Central City, Dr. Sabin went East to become the first woman professor at Johns Hopkins University, Baltimore, and the first woman to be elected to a life membership in the National Academy of Sciences.

FLORIDA

Cardiovascular Seminar in St. Petersburg.—The annual Suncoast and Hillsborough County Cardiovascular Seminar will be held Friday and Saturday, April 3 and 4, at the Tides Hotel and Bath Club, Redington Beach, St. Petersburg. Programs will be presented from 10 a. m. to 5 p. m. each day. This seminar is sponsored jointly by the Suncoast Heart Association, St. Petersburg, and the Hillsborough County Heart Association, Tampa. Seven specialists in various phases of diagnosis, treatment, and surgery in the cardiovascular field will present papers and take part in panel discussions, including Dr. John W. Hurst, Emory University; Dr. John B. Hickam, University of Indiana; Dr. Haddow M. Keith, University of Toronto Medical School; and Dr. Herbert E. Warden, University of Minnesota, Minneapolis. Credit for attending the seminar will be given by the American Academy of General Practice and the sponsoring heart associations cordially invite all physicians to attend. Registration fee

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

is $5. For information, write the Hillsborough County Heart Association, 111 Zack St., Tampa 2, Fla.

IDAHO

Cancer Conference in Boise.—The first annual Idaho Cancer Conference of the American Cancer Society, Idaho Division, will be held in Boise April 10-11 at the Hotel Boise, with physicians, dentists, and nurses participating. Of the six sessions scheduled, the following will be for physicians only, with Dr. Frank W. Crowe, Portland, Ore., presiding:

Diagnosis and Treatment of Cancer of the Uterus, Dr. John A. Wall, Houston, Texas.
Current Problems with Cancer; Polyps of the Colon and Rectum, Dr. Joel W. Baker, Seattle.
Breast Cancer—Treatment, Dr. Frank E. Adair, New York City.
Question-Answer session.
Conclusion, Dr. Crowe.

For information write Dr. Crowe at 116 W. State St., Boise, Idaho.

LOUISIANA

Appoint Dr. Beaver to Professorship.—Paul C. Beaver, Ph.D., was appointed the William Vincent Professor of Tropical Diseases and Hygiene at Tulane University School of Medicine, New Orleans. Dr. Beaver, formerly professor of parasitology, was a member of the medical school faculty since 1945. He succeeds Ernest Carroll Faust, Ph.D., who has reached retirement age but continues as field coordinator of the Tulane consultant program with the seven medical schools of Colombia, South America.

Personal.—Dr. Charles E. Dunlap, chairman, department of pathology, Tulane University School of Medicine, New Orleans, was reelected to a new three-year term on the Board of Directors of the Oak Ridge Institute of Nuclear Studies, Oak Ridge, Tenn. The council of the institute at its annual meeting Oct. 21 also elected Fisk University, Nashville, as its 37th sponsoring university.——Dr. William W. Frye, dean and professor of tropical medicine, Louisiana State University School of Medicine, New Orleans, was appointed to the National Advisory Allergy and Infectious Diseases Council. Since 1946, Dr. Frye has been a special consultant in tropical medicine to the U. S. Public Health Service.

MASSACHUSETTS

Dr. Jailer to Lecture.—The Alpha Omicron chapter of the Phi Delta Epsilon Fraternity will hold its Aaron Brown lectureship series April 3 in the Boston University School of Medicine auditorium. The guest speaker will be Dr. Joseph W. Jailer, department of medicine, Columbia University College of Physicians and Surgeons, New York City. His subject is "Certain Aspects of Hyperadrenalism."

MICHIGAN

Establish Residents' Day for Obstetrics-Gynecology.—An annual "Residents' Day" was established by the department of obstetrics and gynecology at Wayne State University College of Medicine, and the first program was held Feb. 25. All residents in obstetrics and gynecology in Michigan are invited to attend these one-day sessions held at the Wayne County Medical Society auditorium. Dr. Clyde L. Randall, chairman of obstetrics and gynecology, University of Buffalo College of Medicine, was the dinner speaker Feb. 26. Dr. Randall spoke on the "Oophorectomy and the Consequences." During afternoon ward rounds at Receiving Hospital, there was a brief presentation on the "Current Treatment of Pelvic Inflammatory Disease."

Mortality in Child Birth.—The rate at which Michigan women die as a result of childbirth or pregnancy was reduced by 67% in the last 10 years, according to figures released by the Michigan Department of Health. In 1947, 11 Michigan mothers died for every 10,000 babies born alive. In 1957, the rate was 3.8. Provisional figures for the first nine months of 1958 indicate the rate for last year will be below the 1957 figure. To stress the importance of early prenatal care, classes for expectant parents are conducted in 34 Michigan counties. Dr. Charles A. Behney, maternal and child health consultant, Michigan State Health Department, said major causes of maternal deaths today are hemorrhage, toxemia, infection, anesthesia, and heart disease.

Support for Survival Proposition.—Dr. George Moore, regional medical officer, Office of Civil and Defense Mobilization, Battle Creek, announced that "Michigan voters should support Proposition 1 on the state ballot April 6 to assure the survival of the state's government in the event of nuclear attack. Proposition 1 simply modernizes our present Michigan laws so that governments at all levels can carry out their responsibilities to assure the continuity of civilian government . . . judicial, legislative and executive . . . and the continuation of civil law in the event of a nuclear attack. Under this law, the Legislature can provide succession in office, if incumbents are disabled by enemy attack, and can adopt such other measures at county and city levels as is deemed necessary to assure that individual liberties and civil rights of the people will be preserved and protected following an enemy attack upon this Nation. If the amendment is approved by the voters it also provides that elections shall always be called, as soon as possible, to fill any elective vacancies, in any offices, temporarily occupied, due to the incapacity of the lawful elected officials. In effect, the law prepares for continuation of civilian law and order to prevent martial or dictatorial law in time of nuclear war."

MISSOURI

Dr. Wood to Give Annual Lecture.—Dr. W. Barry Wood Jr., vice-president, Johns Hopkins Medical Institutions, Baltimore, will deliver the ninth annual Memorial Lecture at the Menorah Medical Center of Kansas City on Tuesday, May 12. The subject of his lecture will be "The Genesis of Fever." Dinner will be at 6:30 p. m. and the lecture at 8 p. m.

NEW MEXICO

Devote Annual Meeting to Space Medicine.—The annual meeting of the New Mexico Medical Society in Las Cruces, May 5-7, will be devoted exclusively to space medicine, Dr. James C. Sedgwick, president, has announced. A tour and demonstration will be held May 5 at Holloman Air Base, N. M., a few miles from Alamogordo, where the Air Force Missile Development Center, Air Research and Development Command of the U. S. Air Force is located. Sessions on May 6 and 7, held in Milton Hall at New Mexico State University, Albuquerque, will include discussions by guest speakers on research problems in space medicine. Physicians will witness the routine operation of missile testing and may see missiles fired. The following are scheduled to discuss the subjects listed:

Dr. W. Randolph Lovelace, II, Albuquerque, "Crew Selection for Space Flight"; Col. John Pickering, Randolph Air Force Base, San Antonio, Texas, "Radiation Problems in Space Medicine"; Col. John Paul Stapp, Wright Air Development Center, Ohio, "Accelerations in Space Flight"; Major Stanley C. White, Washington, D. C., "Cabin Ecology for Space Flight"; and Capt. George E. Ruff, Wright Air Development Center, Ohio, "Psychophysiology of Space Flight."

Also present will be Dr. F. J. L. Blasingame, Executive Vice-President of the American Medical Association. The Air Force requires that all who plan to go on the conducted tour must preregister by April 15 to be cleared through security. All who have a registration badge will be permitted to board the Air Force buses for the tour, including wives, exhibitors, and guests. The Air Force will not permit private automobiles or cameras. Mail advance registration, with registration fee of $10, to New Mexico Medical Society, 220 First National Bank, Albuquerque, N. M. Room reservation information will be mailed to those who forward registration.

NEW JERSEY

Orthopedic Seminar.—The orthopedic department of St. Joseph's Hospital, Paterson, will hold an orthopedic seminar designed only for residents in orthopedic surgery on Saturday, April 4. Residents who are being trained in New England, New York, New Jersey, Pennsylvania, Delaware, Maryland, and in the District of Columbia are cordially invited. There is no charge. Advance registration is requested. Please address all communications to Dr. R. R. Goldenberg, St. Joseph's Hospital, Paterson, N. J.

NEW YORK

Meeting on Tuberculosis and Health—The annual meeting of the New York Tuberculosis and Health Association, Inc., will be held April 8 at the Hotel Statler Hilton, New York City. Moderator for the scientific and sociologic session will be Dr. John H. McClement, visiting physician-in-charge, chest service Bellevue Hospital. Papers to be presented include:

Tuberculosis Among the Navajo: Research in Cross-Cultural Technologic Development in Health, Dr. Kurt W. Deuschle, Cornell University Medical College.

The Tuberculin Test: An Old Test with a New Look, Dr. Michael L. Furcolow, Kansas City Field Station, U. S. Public Health Service.

Some Observations on the Use of Drugs in the Prevention of Experimental Tuberculosis (Chemoprophylaxis), Dr. Leon H. Schmidt, Christ Hospital, Cincinnati.

At the luncheon session, Dr. Carl Muschenheim, president of the association, will speak, and Dr. Walsh McDermott, Livingston Farrand Professor of Public Health and Preventive Medicine, Cornell University Medical College, will present "The Community's Stake in Medical Research."

Institute on Medical Teaching.—The second Summer Institute on Medical Teaching, jointly sponsored by the University of Buffalo and the Association of American Medical Colleges, will be held in Buffalo June 9-18, 1959. Included in the presentations, demonstrations, and discussions led by University of Buffalo faculty from the schools of medicine, education, and arts and science will be such topics as the nature of learning; the nature of medical students and medical faculties; the philosophical background for higher education in the United States; the use of lecture and laboratory, ward exercise, and clinical conference, as well as less familiar methods of instruction; and the use of tests and other appraisal devices for measuring student performance in a medical school. Opportunity for consultation on individual instructional problems will also be provided. Attendance will be limited. Interested members of Medical School faculties in the United States and Canada may apply for registration or information by writing Dr. George E. Miller, associate professor of medicine, University of Buffalo School of Medicine, Buffalo 14, N. Y.

New York City

Dr. Wilson Wins Prize in Neurology.—Irwin B. Wilson, Ph.D., associate professor of biochemistry, Columbia University, was awarded the annual prize in neurology given by the Association for Research in Nervous and Mental Disease. The prize carries an award of $1,000. Dr. Wilson recently achieved national recognition for his success at designing PAM, antidote against the toxic effects of nerve gas and insecticides. The citation issued by the association commended Dr. Wilson for his antidote and for his "contribution toward man's understanding of the action of toxic gases on the nervous system."

Doctors' Symphony Gives Benefit Concert.—The Brooklyn Doctors' Symphony Orchestra, of which Maurice P. Yuppa, D.D.S., is president, presented a concert on Feb. 20 for the benefit of Student Nurses recruitment program of the Nurses Association of the Counties of Long Island. Physicians, dentists, nurses, and members of allied professions are invited to become members of the orchestra. Rehearsals are held at 8:30 p. m. at The Clara Barton Vocational High School, 901 Classon Ave., Brooklyn. For details contact Dr. Benjamin A. Rosenberg, 909 President St., Brooklyn 15 (Nevins 8-2370).

Vitamin Researcher Celebrates Seventy-Fifth Birthday.—Dr. Casimir Funk, pioneer in vitamin research, marked his 75th birthday Feb. 23. Dr. Funk was born in 1884 in Warsaw, Poland, son of a dermatologist. He received his Ph.D. in organic chemistry from the University of Berne. He then went to the Pasteur Institute in Paris to work with Gabriel Bertrand, reportedly the first professor of biochemistry. At the Lister Institute in London, in 1911, Dr. Funk isolated from rice polishings a substance that cured beriberi. Knowing this substance essential to life, he gave it the name "vitamine," later changed to vitamin. Shortly thereafter, he isolated crystalline nicotinic acid and other vitamin B components from extracts of yeast and rice polishings, and worked out the manner in which thiamine (vitamin B_1) is utilized by the body. In 1923, Dr. Funk was appointed by the Rockefeller Foundation to organize the department of biochemistry at the State School of Hygiene in Warsaw. Since 1947, Dr. Funk and his co-workers at the Funk Foundation for Medical Research, a nonprofit organization, have been engaged in basic research on problems of cancer, diabetes, peptic ulcer, and arthritis.

OREGON

University Gets Million-Dollar Gift.—The University of Oregon Medical School will share equally with Good Samaritan Hospital, Portland, in the proceeds of an estate valued at 2 million dollars, Dr. David W. E. Baird, dean, has announced. The money, from the estate of the late Arthur H. Devers, is mostly in stocks and bonds, with about $100,000 in cash and mortgages. According to the terms of the will, Dr. Baird said, half of the funds, upon the death of Mr. Devers' widow, were to be turned over to the Oregon State Board of Higher Education for the purpose of teaching the subjects of eye, ear, nose, and throat at the University of Oregon Medical School. Mr. Devers, a coffee roasting pioneer, died Sept. 15, 1944. Upon his death a certain number of specific bequests were made and the residue of the estate was held in trust until the death of his widow, Mrs. Anne E. Devers, recently.

PENNSYLVANIA

Plan New Hospital in Media.—Directors planning the new Riddle Memorial Hospital near Media announced the appointment of a Doctor's Advisory Committee, composed of physicians serving on the staffs of other hospitals and clinics in the Philadelphia area. Riddle Memorial will be built largely from funds bequeathed for this purpose by the late Samuel D. Riddle, race-horse owner. It will be built on a 72-acre plot left by Mr. Riddle on Baltimore Pike near Media, to serve the 75,000 people of Central Delaware County. Long range plans include the erection of a modern 150-bed hospital, expandable to 300 beds, a nurses home, doctors offices, and a geriatrics center for research and study in connection with the rapidly growing elderly section of the American population. Cost of the main building, planned to be started in 1960, will be about 5 million dollars.

Philadelphia

Open Laboratory of Cytology.—A symposium on cytology was held Feb. 27 at the Hahnemann Medical College to mark the opening of the new Laboratory of Cytology. The following five pathologists spoke at the symposium: Dr. Cyrus C. Erickson, professor of pathology, University of Tennessee, Memphis; Dr. Irene Koprowska, director, Hahnemann Cytology Laboratory; Dr. Peter A. Herbut, of Jefferson Medical College; Dr. Emerson Day, director, Strang Cancer Prevention Clinic of Memorial Hospital, New York City; and Dr. James W. Reagan, Western Reserve University School of Medicine, Cleveland. Under Dr. Koprowska's direction, the Cytology Laboratory is engaged in a four-fold program. The diagnostic service examines body fluids and secretions for cancer cells. The laboratory is one of about 30 in the country recognized as a teaching center to train pathologists and technicians, and is approved by the Board of Schools of Medical Technologists of the American Society of Clinical Pathologists. The laboratory has been conducting research concerned with chemically-induced cervical carcinoma of mice. In a program supported by the U. S. Public Health Service, it also participates in a cooperative pilot study of the American Cancer Society and the Veterans' Administration concerned with a simultaneous mass population screening by cytologic and radiologic methods for the early detection of cancer of the lung.

VIRGINIA

New Headquarters Building for State Society.—The Medical Society of Virginia recently held an open house in dedication of its new headquarters building at 4205 Dover Road, Richmond. In 1946 the society expanded its work with the employment of the late Mr. Henry S. Johnson as director of public relations and the need for more adequate work space for society executives was apparent. In 1951, a building was purchased at 1105 W. Franklin St., which became the society's official headquarters. Subsequently, a study committee with Dr. Guy W. Horsley, as chairman, recommended that a new headquarters building be erected. This action was approved by the council, the House of Delegates, and the membership at its annual convention in 1956. The maximum sum of $120,000 was appropriated for purchase of the land, erection of the building, and for equipment. A building committee appointed by President James Hagood began its work on Oct. 31, 1956. The present property was acquired from the Richmond Foundation. The new building was completed in September, 1958, and contains a reception area, committee meeting rooms, executive offices, a small kitchen, a conference room, offices where the *Virginia Medical Monthly* work is done, and, on the second floor, the office of the Virginia Academy of General Practice. The land for the building cost $21,000 and the building itself cost $80,000. The total cost including architect's fees, equipment, etc., was just under $116,000. An off-street parking area in front of the building can accommodate 200 cars.

The new headquarters building of the Medical Society of Virginia located in Richmond.

GENERAL

Fellowships in Audiology and Speech.—Opening of competition March 6 for two fellowships in audiology and speech at Northwestern University, Chicago, has been announced by the American Hearing Society, its member agency, the St. Paul Hearing Society, and the university. Winners of the awards, known as the Reine Humbird Myers Fellowships, will receive $3,000 a year for two years while participating in a graduate program in preparation for work in local hearing societies. The fellowships were established in 1957 through a bequest from the Myers Foundation of St. Paul, Minn. Information and applications may be obtained from Crayton Walker, executive director, American Hearing Society, 919 18th St., N. W., Washington 6, D. C. Closing date for returning completed applications to Mr. Walker is April 6.

Biennial Conference on Anesthesiology.—"The Heart and Anesthesia" is the theme for the sixth biennial Western Conference on Anesthesiology to be held April 1-4 at the Westward Ho Hotel, Phoenix, Ariz. The conference will open with an address by Dr. Daniel C. Moore, Seattle, president, American Society of Anethesiologists. The following panel discussions and moderators are planned:

Applications to Clinical Anesthesia, Dr. Stuart C. Cullen, San Francisco.
Practical Use of Monitory Devices—Which, When, How, To Whom?, Dr. Robert D. Dripps, Philadelphia.
The Unsolved Problems of Cardiac Surgery, Dr. Robert W. Virtue, Denver.

A motion picture, "Fluothane," will be shown each day. Entertainment will include tours, golf, swimming, horseback riding, and a ladies' program.

Meeting on Border Public Health.—The United States–Mexico Border Public Health Association will hold its 17th annual meeting in Brownsville-Matamoros, March 30-April 3. During the plenary sessions there will be discussions on the recent progress in public health both in the U. S. and in Mexico, the activities of joint health councils in border communities, the epidemiology and laboratory aspects of arthropod-borne encephalitides, the needs and resources for the training of public health personnel working along the border, the rabies problem in the border area, and the attenuated live poliovirus oral vaccine. Six sessions (maternal-child health, veterinary public health, venereal diseases, nursing, sanitation, and tuberculosis) will meet, some of them in joint meetings. Simultaneous interpretation services will be available in all plenary sessions. For information write the United States-Mexico Border Public Health Association, 243 U. S. Court House, El Paso, Texas.

Psychotherapy Meeting in San Francisco.—The fifth annual Western regional meeting of the American Group Psychotherapy Association will be held April 2-3 in San Francisco at the Sheraton-Palace Hotel. Advances the past year in group psychotherapy will be keynoted in a paper by Dr. Martin Grotjahn, of Beverly Hills, with Mr. S. R. Salvson, of New York City, editor of the *International Group Psychotherapy Journal*, as discussant. More than 17 symposiums, workshops, and general sessions will consider group counseling in a state prison, group therapy programs for family agencies, group psychotherapy for criminal offenders, family group therapy, therapeutic techniques in adolescents' groups, the transactional analysis, treatment of psychotic patients by group methods, and allied subjects. The meeting arrangements are in charge of Dr. Hymen S. Morgenstern, of San Francisco, and Dr. Max A. Sherman, of Beverly Hills, co-chairmen. For information, write Dr. Donald A. Shaskan, VA Mental Hygiene Clinic, 49 Fourth St., San Francisco 3.

Study of Hospital Admissions.—The reason more than 20 million Americans—about 12.5%—enter a hospital each year will be the subject of a study authorized by the executive committee of Health Information Foundation. It will be conducted jointly by the National Opinion Research Center of the University of Chicago and the foundation. A sample of admissions to hospitals in Massachusetts will be examined through the approval and cooperation of the Massachusetts Medical Society, the Massachusetts Hospital Association, and the Blue Cross–Blue Shield Plans in that state. The 2½-year study will attempt to ascertain the nonmedical factors and family situations which lead to hospital utilization as well as medical reasons given by physicians. The survey is one of a group of major studies of voluntary health insurance sponsored by the foundation. The foundation was organized in 1950 as a contribution by the drug, pharmaceutical, chemical, and allied industries to research and education in the social and economic aspects of medical care.

Centennial for Section on Obstetrics and Gynecology.—The Section on Obstetrics and Gynecology of the American Medical Association will commemorate the 100th anniversary of its founding at the A. M. A. meeting in Atlantic City, June 8-12. A special program is being arranged for this occasion, including a commemorative luncheon and an address by Mr. Andrew Claye, of Leeds, England, president of the Royal College of Obstetricians and Gynecologists of Great Britain. Also included are a panel discussion on "Pelvic Exenteration—Current Status" on June 10; a combined meeting June 11 of seven A. M. A. Sections (Pathology and Physiology, Pediatrics, Nervous and Mental Diseases, Anesthesiology, Diseases of Chest, General Practice, Obstetrics and Gynecology) considering "Childbirth—Progress in Management"; June 12, a joint meeting with the Section on Pathology and Physiology, including two panels, "Ovarian Tumors" and "Rh Disease." Hotel reservation forms for this meeting will appear in THE JOURNAL or can be obtained from A. M. A. headquarters, 535 N. Dearborn St., Chicago 10.

Conference on Municipal and Industrial Waste.—The eighth Southern Municipal and Industrial Waste Conference will be held April 2-3 at the University of North Carolina, Chapel Hill. These conferences, organized jointly by Duke University, North Carolina State College, and the University of North Carolina, are for the purpose of bringing together representatives of industry, municipalities, and governmental agencies responsible for developing policies relating to the preservation of water resources in the southeastern part of the U. S. The eighth conference will be devoted to techniques available in the treatment of municipal and industrial waste waters. General sessions will be devoted to "solids separation processes," "chemical and biological treatment," and "solids handling and disposal." Formal papers will be followed by prepared discussions and by an informal discussion. Registration fee is $15 and includes attendance at all sessions, a copy of the conference *Proceedings*, two luncheons, and the social hour and banquet. For information write the University of North Carolina School of Public Health, Department of Sanitary Engineering, Chapel Hill, N. C.

Meeting on Physical Medicine in New Haven.—The Eastern Section of the American Congress of Physical Medicine and Rehabilitation will meet April 18 at the Yale University School of Medicine, New Haven, Conn. The program includes the following:

Connective Tissue Massage, Dr. Morton Hoberman, New York City.
Stretching, Dr. Thomas F. Hines, New Haven.
Proprioceptive Facilitation, Dr. Herman Kabat, Providence, R. I.
First Publications in Physical Medicine, Dr. John F. Fulton, New Haven.
Comparative Values of Electrodiagnosis and Electromyography, Dr. W. T. Liberson, Chicago.
Skin Thermometry in the Diagnosis of Peripheral Vascular Diseases, Alfred Ebel, New York City.
Importance of Leg Length in Low Back Pain, Dr. Harold Lefkoe, Philadelphia.
The Third International Congress of Physical Medicine, Dr. Frank H. Krusen, Rochester, Minn.
Trends in Medical Education, Dr. Vernon S. Lippard, dean, Yale University School of Medicine.

Parts of the program will be chaired by Drs. Robert C. Darling, of New York City, and Ernst Fischer, of Richmond. For information write Dr. Sidney Lich, 360 Fountain St., New Haven 15, Conn., secretary.

General Practice Meeting in San Francisco.—The American Academy of General Practice will hold its 11th annual scientific assembly April 6-9 in San Francisco's Civic Auditorium. The scientific program will feature 28 physician-speakers. More than 100 scientific and 300 technical exhibits are planned. The Congress of Delegates will convene at 2 p. m., April 4, in the Fairmont Hotel. Opening ceremonies at 1 p. m., April 6, include a call to order by Dr.

Holland T. Jackson, Fort Worth, Texas, president of the academy. Dr. Walter H. Judd, U. S. Congressman from Minnesota, will speak on "Doctors in a Changing World." Other participants include Dr. Leroy E. Burney, surgeon general, U. S. Public Health Service, presenting "Public Health: Its Relation to the Practice of Medicine," and James H. Steele, D.V.M., U. S. Public Health Service, who will give "Animal Diseases Transmissible to Man." The president's reception is planned for the evening of April 8. A ladies' program is arranged, and postassembly plans include the Invitational Scientific Congress April 13-14 in Honolulu, Hawaii. For information write The American Academy of General Practice, Volker Boulevard at Brookside, Kansas City 12, Mo.

Pediatricians Meeting in San Francisco.—The American Academy of Pediatrics will hold its spring session at the Sheraton-Palace Hotel, San Francisco, April 13-15. The general sessions and exhibits will be held at the hotel, and afternoon clinics will be conducted in four of the pediatric departments in the Bay Area, April 15. A "Conference on Respiratory Problems of the Newborn" will be moderated by Dr. Moses Grossman, San Francisco, April 13. The following panel discussions and moderators are scheduled:

Inborn Errors of Metabolism, Dr. Ruth Gross, San Francisco.
Some Current Problems in Infectious Diseases, Dr. Henry B. Bruyn, San Francisco.
Problems in Growth and Development, Dr. Donald Pickering, Portland, Ore.
Abdominal Surgical Problems in Pediatrics, Dr. Edward B. Shaw, San Francisco.
Adolescence—The Pediatrician's Problem, Dr. Arthur Roth, Oakland.
Clinical Pediatric Allergy, Dr. John P. McGovern, Houston, Texas.

Entertainment includes the banquet April 14, 8 p. m. ($7.50), and a ladies' program. For information write the American Academy of Pediatrics, P. O. Box 1116, Evanston Ill., Dr. E. H. Christopherson, Executive Secretary.

Meeting on Sterility in Atlantic City.—The 15th annual meeting of the American Society for The Study of Sterility will be held at the Shelburne Hotel, Atlantic City, N. J., April 3-5. The secretary of the society is Dr. Herbert H. Thomas, 920 S. 19th St., Birmingham 5, Ala., and the president of the society for 1959 is Dr. Edward C. Reifenstein Jr., New Brunswick, N. J. On April 3 the Squibb prize paper from the 1958 annual meeting of the Pacific Coast Fertility Society, "The Endocrine Control of the Passage of Spermatozoa and of Ova Through the Female Genital Tract," will be given by Dr. Robert W. Noyes, department of obstetrics and gynecology, Stanford University School of Medicine, San Francisco. On April 5 Dr. Peter M. F. Bishop will give the Ayerst Lecture, "Cervical Mucus." Dr. Bishop is from the department of obstetrics and gynaecology, Postgraduate Medical School, Guy's Hospital, and Chelsea Hospital for Women, London, England. The presidential address, "Nolle Nodere," will be presented by Dr. Sheldon A. Payne, The Shelton Clinic, Los Angeles, and the Fred A. Simmons Memorial Address, "Experience, Experiment, and Error in Sterility," by Dr. Alan N. B. Grant, department of gynaecology, Women's Hospital, Sydney, Australia.

Neurology Meeting in Los Angeles.—The 11th annual meeting of the American Academy of Neurology will be held April 13-18 at the Statler-Hilton Hotel, Los Angeles, under the presidency of Dr. Francis M. Forster, Madison, Wis. Special courses will be conducted April 13-15. The S. Weir Mitchell Award Essay is scheduled for the morning session of April 16. Papers to be presented by foreign participants are as follows:

Some Features of the Pathogenesis of Myotonia, N. I. Grashchenkov, Moscow, U.S.S.R.
Electrophysiological Study of Cortical and Spinal Cord Lesions in Cats with Allergic Encephalomyelitis, Roger M. Morrell, Montreal, Quebec.
Injury to the Nervous Tissue Produced by Intracarotid Injection of Alcohol, J. Olszewski and B. Rozdilskyi, Saskatoon, Saskatchewan.
Electron Microscope Study on the Function of Astroglia in the Water Ion Metabolism of the CNS, H. M. Gerschenfeld, F. Wald, J. A. Zadunaisky, and E. De Robertis, Buenos Aires, Argentina.

A symposium on rhinencephalon the morning of April 17 will have Dr. Ray S. Snider, of Chicago, as chairman. A joint meeting of the sections of neurochemistry and neuropharmacology will be held. Eighty-six papers are scheduled for presentation at the scientific sessions, and over 70 papers will be read by title. Scientific, society, and commercial exhibits and demonstrations and movies are planned. For information write the American Academy of Neurology, 4307 E. 50th St., Minneapolis 17.

Fellowships for Study of Human Ecology.—A grant from the estate of Anne Parrish Titzell, professor of medicine (neurology), Cornell University Medical College, New York City, made possible the establishment of fellowships for those interested in the study of human ecology and its relation to health. An immediate purpose is to provide opportunities for study and investigation for men who plan to pursue academic careers. Three general areas are within the scope of the program: the investigation of the social and physical milieu in which men live, and the attempt to learn more about how specific aspects of this milieu affect health and behavior; the investigation of the interaction between men and their milieu, and of how a man's perception of his life situation influences his reaction to it; the investigation of the interaction between bodily processes and the highest integrative activities of the brain, and the relevance of this to specific disease syndromes. Dr. Lawrence E. Hinkle Jr. will be associated with Dr. Harold G. Wolff in the direction of the program. The staff includes representatives from internal medicine, psychiatry, neurology, psychology, sociology, and cultural anthropology. Fellows will have an opportunity to participate in field observations of groups drawn from the general population, to take part in the long-term observation and care of out-patients in a research facility especially designed for this purpose, and to make use of laboratory facilities for the study of behavior, and of processes relating to the functions of various organ systems. Three fellowship appointments will be made annually each for a term of two years. Applicants should have completed one or more years of postgraduate training in the fields of internal medicine, neurology, psychiatry, preventive medicine, or public health. The stipend allowed is $4,500 the first year, and $5,000 the second; an additional allowance of $500 per annum is made for each dependent. To make application, write to Dr. E. Hugh Luckey, Chairman of the Department of Medicine, New York Hospital-Cornell Medical Center, 525 E. 68th St., New York 21.

CANADA

Surgeons Meet in Montreal.—A sectional meeting of the American College of Surgeons will be held April 6-9 at the Queen Elizabeth Hotel, Montreal. More than 15 symposiums are planned, and the following panel discussions and moderators are scheduled:

Biliary Tract Surgery, Dr. Richard B. Cattell, Boston.
Discussion on Activities of the College, Dr. Paul R. Hawley, Chicago, director of the college.
Angioplastic Procedures in the Management of Peripheral Arterial Occlusive Disease, Dr. D. Emerick Szilagyi, Detroit.
Anesthesia for Surgery, Dr. Louis Lamoureux, Montreal.
Medicolegal Aspects of Trauma, Dr. Alexander P. Aitken, Boston.
Cardiovascular Surgery, Dr. David R. Murphy, Montreal.
Fractures of Neck of Femur, Dr. J. Gordon Petrie, Montreal.

Dr. L. G. Stevenson, dean, Faculty of Medicine, McGill University, will present an address at the dinner of the Montreal Ophthalmological Society, 7 p. m., April 6. A round-table conference on detachment of the retina will be moderated by Dr. Samuel T. Adams, Montreal, April 7. At the college dinner 7 p. m., April 8, with Dr. Newell W. Philpott, Montreal, president of the college, presiding, Mr. Hugh MacLennan, Montreal, will be the speaker. Section meetings, motion pictures, and exhibits are arranged.

LATIN AMERICA

Nutrition Institute Founded in Mexico City.—A new, autonomous National Institute of Nutrition, comprising the Hospital for Nutritional Diseases, the Directorate of National Nutrition, and a Division of Research and Training, was organized by the government of Mexico. To help support research in biochemistry and nutrition at the institute, the Rockefeller Foundation appropriated $90,000 for use over a three-year period. The Hospital for Nutritional Diseases, established in the early 1940's, has contributed to medical training and research and to hospital care in Mexico. The Directorate of National Nutrition is responsible for community and public health aspects of nutrition. Studies undertaken by the directorate are being supported by the Mexican Department of Health with assistance received under a cooperative agreement with the World Health Organization, the United Nations International Children's Emergency Fund, and the Food and Agriculture Organization. The chief unit of the Division of Research and Training is the department of biochemistry. A staff, headed by Dr. Guillermo Soberon, has been formed, and a two-year course leading to the National University of Mexico's master's degree has been started. Initially, the biochemical research will focus on three main topics: the development of better methods for determining nutritional status; the nutritional value of Mexican foods; and protein metabolism, including the utilization of proteins and amino acids in Mexican foods.

FOREIGN

Spain's "Oldest Doctor" Dies.—The San Antonio *Light* reported that Dr. Jose Amo Serrano, reportedly Spain's oldest doctor, died in Cordoba, Spain, Jan. 9. Dr. Serrano had remained active in his profession until he was 100.

British and Irish Surgeons Meet in London.—The annual meeting of the Association of Surgeons of Great Britain and Ireland will be held April 23-25 in London under the presidency of Prof. Sir James Paterson Ross with the following papers scheduled:

Acute Pancreatitis.
Clinical Diagnosis in Chronic Pancreatitis.
Chronic Pancreatitis.
Islet-cell Tumors of the Pancreas.
Genito-urinary Tuberculosis.
Bone Tuberculosis.
Tuberculous Lymphadenitis.

A Moynihan Lecture at the Royal College of Surgeons will follow an afternoon of films, April 24, on which evening will be held the annual dinner. The Honorary Secretary of the Association is Mr. Rodney Smith, 47 Lincoln's Inn Fields, London, W. C. 2.

British Association for Medical Education.—The Association for the Study of Medical Education in Great Britain, organized late in 1957 to serve as a forum for persons interested in the problems of medical education and as a clearinghouse for information on the field, will be assisted during its initial, developmental years by a grant of £10,000 (about $28,500) from the Rockefeller Foundation to the Royal College of Physicians, London. The major purposes of the association are to exchange information on medical education in Great Britain, organize meetings on relevant topics, maintain a bureau where information can be received, stored, and made available to those interested, and encourage, promote, or conduct research into matters concerned with medical education. It is free to initiate other activities which it decides will advance the interests of medical education. Almost all the licensing bodies and medical schools of Great Britain, as well as individual medical educators and practitioners, are members of the new association.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral.* Phoenix, April 5-10. Applications now on file. *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application was Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Public Health.* Minneapolis, Boston, Baltimore, Chapel Hill, North Carolina and New Orleans, April 9-11; Berkeley, Calif., April 23-25; Pittsburgh, April 16-18. *Occupational Medicine.* Chicago, April 24-26. *Aviation Medicine.* Los Angeles, April 24-26. Final date for filing all applications is March 16. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. *Final date* for filing application is July 1. *Oral.* September. *Final date* for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

NAVY

Captain Schiff Honored.—Capt. Maurice Schiff, chief of the eye, ear, nose, and throat service at the U. S. Naval Hospital, Oakland, Calif., was selected as the 1959 recipient of the Harris P. Mosher Memorial award, an honor that comes in connection with his election to active fellowship in the American Laryngological, Rhinological, and Otological Society, Inc. The organization confers this honor each year on the candidate who submits the best thesis. "Juvenile Nasopharyngeal Angiofibroma" was the title of Captain Schiff's thesis. Dr. Schiff presented his paper at the annual meeting of the society in Hot Springs, Va., on March 12. The honor carries with it a Harris P. Mosher Memorial award certificate, the listing of the recipient's name on the scroll published each year in the annual program of the society, 100 complimentary copies of the prize thesis, and its submission for consideration for publication in a forthcoming issue of *Laryngoscope.*

PUBLIC HEALTH SERVICE

Research Training Program.—Seventeen countries of Central and South America and Australasia will participate in the Public Health Service's international research training program. The program, which was started a year ago, provides medical research training in the United States for scientists from abroad. With the 17 new participants (Argentina, Australia, Brazil, Ceylon, Chile, Columbia, El Salvador, India, Iran, Japan, Mexico, New Zealand, Pakistan, Peru, Philippine Islands, Thailand, and Uruguay), 30 countries are now participating in the program. A research fellowship review panel of scientists has been established in each country. Within each nation, candidates are nominated by its scientific panel, and final recommendations for the awards from the Public Health Service are made by a research fellowship board of the National Institutes of Health.

The chairman of the fellowship board is Dr. John R. Paul, professor of preventive medicine at Yale University, who, with Dr. Ronald E. Scantlebury of the National Institutes of Health, served as advisor to the participating countries in setting up their review panels and in entering the program. In 1958, through similar panels, applications resulting in 17 awards were received from Austria, Belgium, Denmark, England, Finland, France, Germany, Holland, Italy, Norway, Spain, Sweden, and Switzerland. The 17 research fellows are now doing research in medical centers in the United States. Each fellow holds a doctoral degree or its equivalent in one of the medical or related sciences and has demonstrated promise in research. All have a workable knowledge of English. The training of these scientists from other countries will strengthen medical research throughout the world and will give outstanding scientists a chance to share knowledge with kindred groups by conducting research in the United States. Under the program, the Public Health Service provides a basic annual stipend of $4,500, allowances for wives and children, and limited travel funds. Information about the program may be obtained from Dr. Ronald E. Scantlebury, Chief, Foreign Grants and Awards, Division of Research Grants of the National Institutes of Health, Bethesda 14, Md.

New Publications.—A monograph entitled "Morbidity from Cancer in the United States" (PHS publication no. 590) by Harold F. Dorn, chief, Biometrics Branch, Division of Research Services, National Institutes of Health, and Sidney J. Cutler, Head, Clinical Biometry Section, Biometrics Branch, National Cancer Institute, is now available. Part 1 which was published separately, in 1955, deals with variations in the incidence of cancer by age, sex, race, marital status, and geographic region. The current publication completes the 10-city analysis and combines the analysis contained in part 1 with that in part 2, which deals with intercity variation in cancer incidence, trends in cancer morbidity, the association of cancer incidence and income class, and stage of disease at diagnosis. The study represents a statistical analysis of thousands of cancer cases examined in 10 large population centers in the United States which were surveyed in 1937-1939 and resurveyed 10 years later. The areas studied were Atlanta, Ga., Birmingham, Ala., Dallas, Texas, New Orleans, San Francisco, Denver, Chicago, Detroit, Philadelphia, and Pittsburgh. The book can be had by writing to the Superintendent of Documents, Government Printing Office, Washington 25, D. C. The price is $1 per copy.

The new training manual entitled "The Industrial Environment—Its Evaluation and Control" (PHS publication no. 614) is a syllabus of the short courses offered for industrial hygiene engineers and chemists at the Occupational Health Field Headquarters of the PHS in Cincinnati, Ohio. It is devoted primarily to fundamental principles and methods used in the evaluation and control of the working environment. It incorporates comprehensive reference materials, lecture outlines covering such areas as sampling analysis and engineering control measures, and laboratory exercises used in the courses. It includes a special section dealing with specific occupational health problems and their solutions. It is offered for sale by the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at $2.75 per copy.

DEATHS

Ackerman, Emma Malinda Ⓜ Sioux City, Iowa; Creighton University School of Medicine, Omaha, 1913; for many years associated with the Florence Crittenton Home; on the staffs of the Lutheran and Methodist hospitals; died Jan. 14, aged 73.

Baranco, Raymond M., Baton Rouge, La.; Meharry Medical College, Nashville, Tenn., 1912; veteran of World War I; medical director of the Southern University and Agricultural and Mechanical College; a past-president of the Louisiana Medical, Dental and Pharmaceutical Association; died in Our Lady of the Lake Hospital Dec. 19, aged 68.

Baskett, Edgar Drane Ⓜ Columbia, Mo.; Johns Hopkins University School of Medicine, Baltimore, 1919; specialist certified by the American Board of Internal Medicine; served on the faculty of the University of Missouri; formerly on the staff of the Veterans Administration Hospital in Poplar Bluff; died in Dadeville, Ala., Dec. 31, aged 67.

Bein, Philmour Murray Alexis Ⓜ Mansfield, Ohio; University of Pennsylvania School of Medicine, Philadelphia, 1932; interned at the Philadelphia General Hospital; served a residency at the Jewish Hospital in Cincinnati; veteran of World War II; specialist certified by the American Board of Surgery; fellow of the International College of Surgeons; member of the Industrial Medical association; plant physician of Westinghouse Electric Corporation and medical director of the Ingersoll-Humphreys Division, Borg Warner Corporation; associated with the People's and Madison hospitals, and the Mansfield General Hospital, where he died Jan. 9, aged 52.

Berman, Leo, Newton, Mass.; born in Brooklyn April 13, 1913; Universitat Bäsel Medizinische Fakultät, Switzerland, 1937; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology, Inc.; interned at the Lincoln Hospital in New York City; served a residency at the Bellevue Hospital in New York City, Butler Hospital in Providence, R. I., and the Boston State Hospital; member of the American Psychoanalytic Association and the American Psychiatric Association; on the faculty of Harvard Medical School in Boston, where he was on the staff of the Beth Israel Hospital; died Dec. 27, aged 45.

Bostwick, William Warren Ⓜ White Plains, N. Y.; Bellevue Hospital Medical College, New York City, 1894; veteran of World War I; died Jan. 11, aged 85.

Bradford, Stella Stevens Ⓜ Montclair, N. J.; Cornell University Medical College, New York City, 1902; member of the American Rheumatism Association; for many years associated with the Mountainside Hospital, where she was director of the physical medicine and rehabilitation department; died in New York City Jan. 20, aged 87.

Chilton, James C. Ⓜ Hannibal, Mo.; Beaumont Hospital Medical College, St. Louis, 1891; served as division surgeon and examiner for the Wabash Railroad and surgeon for the Chicago, Burlington and Quincy Railroad for many years; chief surgeon for the Universal Atlas Cement Company; associated with St. Elizabeth Hospital and the Levering Hospital, where he died Jan. 11, aged 92.

Collins, James Newton Ⓜ Indianapolis; Emory University School of Medicine, Atlanta, 1922; assistant professor of radiology, Indiana University School of Medicine; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society, the Radiological Society of North America, and the American College of Radiology; past-secretary of the Indiana Roentgen Society; on the staffs of the St. Vincent's Hospital and the Methodist Hospital, where he died Jan. 3, aged 62.

Cooper, Harry Bryant, Mill Valley, Calif.; University Medical College of Kansas City, Mo., 1899; went to Hawaii in 1905 to attend to the medical needs of sugar plantation workers and remained in the islands for 50 years; served on Selective Service boards during World Wars I and II; died Jan. 16, aged 85.

Daly, William Harvey Jr. Ⓜ Killeen, Texas; University of Tennessee College of Medicine, Memphis, 1949; interned at Methodist Hospital in Memphis, Tenn.; formerly a resident at the Scott and White Hospital in Temple, Texas; served as vice-president of the Bell County Medical Society; associated with Burow Clinic and Hospital; died in the Scott and White Hospital in Temple Jan. 8, aged 33.

Deem, Hamlin Nichleson, Wheeling, W. Va.; Ohio Medical University, Columbus, 1901; veteran of World War I; died in the Veterans Administration Hospital, Pittsburgh, Jan. 14, aged 82.

Deruha, John, New Rochelle, N. Y.; Magyar Királyi Påzmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1920; died in New York City Jan. 16, aged 65.

Ⓜ Indicates Member of the American Medical Association.

De Salvo, Francis, Wausaukee, Wis.; Chicago College of Medicine and Surgery, 1917; served as health officer of Wausaukee for many years and member of the school board; at one time health officer of Niagara; died Jan. 26, aged 67.

Dozier, Joseph Vincent, Premont, Texas; Baylor University College of Medicine, Dallas, 1911; veteran of World War I; died Jan. 6, aged 82.

Elles, Norma Bertha Ⓜ Kalamazoo, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1906; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the American Ophthalmological Society; served on the faculty of Baylor University College of Medicine in Houston, Texas, where she was on the staffs of the Hermann Hospital, Memorial Hospital, and the Jefferson Davis Hospital; died in Houston, Texas, Jan. 12, aged 74.

Fasser, Alexander Otto Ⓜ Fremont, Neb.; Yale University School of Medicine, New Haven, Conn., 1905; veteran of World War I; died Jan. 14, aged 79.

Fenimore, William Nolan Ⓜ Wilmington, Del.; Jefferson Medical College of Philadelphia, 1921; veteran of World Wars I and II; served as coroner's physician; died Jan. 5, aged 72.

Hayes, Edwin Patrick Ⓜ Eau Claire, Wis.; born in Richfield Sept. 24, 1886; Marquette University School of Medicine, Milwaukee, 1913; past-president of the Eau Claire County Medical Society and the Tenth District Medical Society; served overseas during World War I; member of the American College of Obstetricians and Gynecologists and the Wisconsin Society of Obstetricians and Gynecologists; one of the founders of the Eau Claire Clinic, which was organized in 1921; on the staffs of the Luther and Sacred Heart hospitals; for 13 years director of Associated Hospital Service, Inc.; past-president of the Eau Claire Rotary Club; died in the Sacred Heart Hospital Dec. 26, aged 72.

Holland, John Gill Ⓜ Lynchburg, Va.; University of Tennessee College of Medicine, Memphis, 1933; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; president-elect of the Lynchburg Academy of Medicine; veteran of World War II; on the staffs of the Virginia Baptist, Lynchburg and Memorial hospitals; died Dec. 24, aged 56.

Horn, Dora L., Winter Park, Fla.; Cleveland Homeopathic Medical College, 1906; died Dec. 19, aged 75.

Hubbard, Milton E. Ⓜ San Francisco; University of Illinois College of Medicine, Chicago, 1928; veteran of World War II; retired from the Veterans Administration Feb. 19, 1957; died Dec. 24, aged 65.

Hutner, Louis Ⓜ Jamaica, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1934; specialist certified by the American Board of Dermatology and Syphilology; on the staff of the Queens General Hospital, where he died Dec. 15, aged 57.

Johnson, William Alexander, Reidsville, N. C.; North Carolina Medical College, Charlotte, 1907; member of the Medical Society of the State of North Carolina; died in the Moses H. Cone Memorial Hospital, Greensboro, Dec. 5, aged 76.

Keever, Henry Floyd Ⓜ Auburndale, Mass.; Harvard Medical School, Boston, 1908; associated with the Newton-Wellesley Hospital, where he served as a trustee; trustee at Lasell Junior College; died Dec. 26, aged 84.

Kells, Paul Ⓜ Miami, Fla.; University of Virginia Department of Medicine, Charlottesville, 1930; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association; veteran of World War II; on the staffs of St. Francis Hospital in Miami Beach and Mercy and Jackson Memorial hospitals; died Dec. 29, aged 56.

Koehler, Malcolm Harvey, Newark, Ohio; Ohio Medical University, Columbus, 1900; served as county coroner; formerly a medical examiner for the Baltimore and Ohio Railroad; died Dec. 29, aged 84.

Krohn, Morris Jacob Ⓜ Denver; University Medical College of Kansas City, Mo., 1903; on the staffs of St. Joseph's Hospital and the General Rose Hospital, where he died Dec. 26, aged 80.

Lamb, Ray Floyd Ⓜ Casa Grande, Ariz.; Northwestern University Medical School, Chicago, 1947; member of the American Academy of General Practice; formerly an officer in the medical corps of U. S. Army Reserve; died Dec. 23, aged 36.

Landes, William Latimer Small Ⓜ York, Pa.; Jefferson Medical College of Philadelphia, 1916; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; veteran of World War I; an honorary member of the radiological staff of the York Hospital; on the board of directors of the Western National Bank; died Dec. 21, aged 67.

Lawn, Hugh Edward, Chicago; St. Louis College of Physicians and Surgeons, 1923; veteran of World War I; affiliated with the South Shore Hospital; died in the Veterans Administration Hospital in Hines, Ill., Dec. 22, aged 63.

Leighton, Adam Phillips Ⓜ Portland, Maine; born in Portland Jan. 23, 1887; Medical School of Maine, Portland, 1910; for many years member and secretary of the Maine Board of Registration of Medicine; past-president of the Maine Medical Association, Cumberland County Medical Society, and the New England Obstetrical and Gynecological Society; in 1945-1946 was president of the Federation of State Medical Boards, of which he was formerly vice-president; since 1948 a member of the National Board of Medical Examiners as a representative of the Federation, and a member of the executive committee; specialist certified by American Board of Obstetrics and Gynecology; fellow of the American Association of Obstetricians and Gynecologists and the International College of Surgeons; served as chairman of the Portland City Council and member of the Board of Alderman, and school board; veteran of World War I; in 1912 established the Dr. Leighton Private Maternity Hospital; associated with the Pownal (Vt.) State School, St. Andrews Hospital in Boothbay Harbor, Webber Hospital in Biddeford, Maine General Hospital, and the Maine Eye and Ear Infirmary, of which he was a trustee; died Dec. 26, aged 71.

McClosky, Ben Martin Ⓜ Tampa, Fla.; Ohio State University College of Medicine, Columbus, 1927; member of the American Academy of General Practice; served as city and county physician; veteran of World War II; died Dec. 10, aged 57.

McDavid, John Solomon Ⓜ Oak Park, Ill.; Northwestern University Medical School, Chicago, 1924; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; on the staffs of the Cook County and Children's Memorial hospitals in Chicago and the West Suburban Hospital, where he died Jan. 4, aged 60.

Mieczkowski, Stanislaus C., Worcester, Mass.; Maryland Medical College, Baltimore, 1912; formerly police surgeon; died in St. Anthony's Hospital, St. Petersburg, Fla., Dec. 23, aged 70.

Miller, Brownlow Bartley, Tabor, Iowa; University of Nebraska College of Medicine, Omaha, 1908; served on the staffs of the Mercy Hospital in Council Bluffs, and Bishop Clarkson Memorial Hospital in Omaha; died Dec. 22, aged 73.

Moore, Edwin Fletcher Ⓜ Cincinnati; Ohio–Miami Medical College of the University of Cincinnati, 1912; member of the American Academy of General Practice; on the staff of St. Francis Hospital; died Dec. 29, aged 69.

Moran, Michael David Ⓜ Farmington, N. M.; Washington University School of Medicine, St. Louis, 1917; veteran of World War I; died in Albuquerque, Dec. 19, aged 66.

Morrison, Whitelaw Reid, Oberlin, Ohio; Columbia University College of Physicians and Surgeons, New York City, 1914; for many years on the faculty of Oberlin College, where he was professor emeritus; at one time associated with the University of Cincinnati; for many years served as chairman of the Lorain County Health Board; taught for two years at a Chinese government school in Shanghai; joint author of "Normal and Elementary Physical Diagnosis"; died in the Allen Memorial Hospital Dec. 26, aged 72.

Motley, Robert William, Tulsa, Okla.; (licensed in Oklahoma in 1916); on the staff of the Moton Memorial Hospital, where he died Dec. 30, aged 77.

Munger, Louis P. Ⓜ Hart, Mich.; Hering Medical College, Chicago, 1895; founder of the Oceana Hospital, where he was a member of the executive board until 1956; for 12 years member of the city council; vice-president of the Oceana County Savings Bank; associated with the Oceana Canning Company of Shelby for many years, and was chairman of the board of directors; died Dec. 23, aged 85.

Myers, Thomas Ⓜ Huntington Park, Calif.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1914; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; formerly on the faculty of his alma mater and the College of Medical Evangelists in Loma Linda and Los Angeles; affiliated with Mission Hospital in Huntington Park, Los Angeles County General and the White Memorial hospitals in Los Angeles, and St. Francis Hospital in Lynwood, where he died Dec. 19, aged 67.

Nickerson, Anson LeRoy Ⓜ Kankakee, Ill.; Rush Medical College, Chicago, 1904; served as secretary of the Kankakee County Medical Society; past-president of the Kankakee County Tuberculosis Association, of which he secretary; veteran of World War I; on the staff of the Kankakee State Hospital; on the honorary staff of St. Mary's Hospital, where he died Dec. 25, aged 81.

Norviel, Herald Bernard Ⓜ Phillips, Wis.; University of Illinois College of Medicine, Chicago, 1920; past-president of the Price–Taylor Counties Medical Society; on the staff of Park Falls (Wis.) Hospital; died Dec. 7, aged 64.

Okrainetz, Clara Loewenherz Ⓜ New York City; Thüringische Landesuniversitat Medizinische Fakultät, Jena, Thuringia, Germany, 1925; specialist certified by the American Board or Radiology; member of the Radiological Society of North America and the American College of Radiology; associated with the Manhattan Eye and Ear Hospital and the Montefiore Hospital, where she died Dec. 25, aged 58.

Osheroff, Samuel A. Ⓜ San Diego, Calif.; University of Nebraska College of Medicine, Omaha, 1919; affiliated with Scripps Memorial Hospital in La Jolla; died Dec. 26, aged 70.

Paisley, Ralph Clifton, Loudonville, Ohio; Ohio State University College of Medicine, Columbus, 1930; veteran of World War II; died Dec. 24, aged 54.

Ransom, Charles Loren, Danville, Va.; born in Syracuse, N. Y., Feb. 1, 1920; Syracuse University College of Medicine, 1945; certified by the National Board of Medical Examiners; specialist certified by the American Board of Urology; vice-president of the Virginia Urologic Society; interned at St. Joseph Hospital in Syracuse, N. Y., and Johns Hopkins Hospital in Baltimore, where he served a residency in urology; served on the faculty of Johns Hopkins University School of Medicine in Baltimore and the State University of New York College of Medicine in Syracuse, N. Y.; on the faculty of the Bowman Gray School of Medicine of Wake Forest College in Winston-Salem, N. C., veteran of World War II; associated with the Danville Memorial and Winslow hospitals; died Dec. 14, aged 38.

Reed, William Wallace Ⓜ Topeka, Kan.; born in Mosinee, Wis., April 1, 1880; Kansas Medical College, Medical Department of Washburn College, Topeka, 1905; specialist certified by the American Board of Otolaryngology; served as president of the Shawnee County Medical Society; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; served as state supervising ophthalmologist for the division of service for the blind of the Kansas State Board of Social Welfare; veteran of World War I; on the staffs of Stormont-Vail and St. Francis hospitals; died Dec. 22, aged 78.

Reynolds, Grover C. Ⓜ Brundidge, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; died Dec. 26, aged 74.

Rifici, Charles, Camden, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1929; served as physician for the Camden City Highway Department, physician for local board number 9 of Selective Service, city physician, and medical inspector of public schools; died in West Jersey Hospital Dec. 22, aged 56.

Riley, Philetus Holt Ⓜ Madison, N. J.; New York Medical College and Flower Hospital, New York City, 1937; certified by the National Board of Medical Examiners; on the staff of the Morristown Memorial Hospital, where he died Dec. 28, aged 53.

Scott, Kenneth Hazen Ⓜ Plainfield, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1942; veteran of World War II; on the staff of the Muhlenberg Hospital; died Dec. 25, aged 43.

Sher, David Daniel Ⓜ Miami Beach, Fla.; Boston University School of Medicine, 1934; certified by the National Board of Medical Examiners; veteran of World War II; formerly practiced in Marlboro, Mass., where he was on the staff of the Marlborough Hospital; died Dec. 12, aged 52.

Simons, Edwin J. Ⓜ Edina, Minn.; born in St. Paul June 23, 1896; University of Minnesota Medical School, Minneapolis, 1924; member of the American College of Chest Physicians; fellow of the American College of Physicians and International College of Surgeons; veteran of World War I; executive director of Minnesota Blue Shield (Minnesota Medical Services) and one of its founders; past-president of the Minnesota State Medical Association; a director of the Minnesota Public Health Association; received a distinguished alumni award in 1956 from the board of regents of the University of Minnesota; for many years practiced in Swanville, where he served as president of the First National Bank; served on the staff of St. Gabriel's Hospital in Little Falls; author of "Primary Carcinoma of the Lungs"; died Dec. 11, aged 62.

Slaney, Andrew F. Ⓜ Oconto, Wis.; Loyola University School of Medicine, Chicago, 1917; veteran of World War II; for many years city health officer; on the staff of the Oconto County and City Hospital, where he died Dec. 19, aged 66.

Stern, Robert Leo Ⓜ Beverly Hills, Calif.; Rush Medical College, Chicago, 1934; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; deputy chief, hospital section, Los Angeles County Civil Defense Commission; on the attending staff, Cedars of Lebanon Hospital; on the staff of the Mount Sinai Hospital; past-president of the Beverly Hills Branch of the Los Angeles County Medical Association; died Dec. 17, aged 50.

Stevens, William Leary Ⓜ Shiloh, N. C.; University College of Medicine, Richmond, 1912; past-president of the First District Medical Society; served as health officer of Camden County; for 17 years medical advisor for the local board Selective Service; died in the North Carolina Memorial Hospital, Chapel Hill, Dec. 23, aged 70.

Stratton-Michener, Sina, Drexel Hill, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1895; served on the staff of the Pennsylvania Hospital in Philadelphia; died in Yeadon Dec. 16, aged 94.

Strother, Rodolph, Oberlin, La.; Memphis (Tenn.) Hospital Medical College, 1903; died Dec. 25, aged 76.

Tamraz, John Moorhaj Ⓜ Colonel, U. S. Army, retired, Miami, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1917; entered the regular Army in 1920; retired May 31, 1949; veteran of World War I; during World War II was chief surgeon in the China-Burma-India Theater and received the Legion of Merit for exceptionally meritorious conduct in the performance of outstanding service; fellow of the American College of Surgeons; died near Richmond, Ga., Dec. 8, aged 69.

Tan, Gilbert Wai Man, Sacramento, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1957; city schools physician; interned at the Sacramento County Hospital, where he served a residency, and where he died Dec. 5, aged 31.

Taylor, Jackson Phyromn Ⓜ Los Angeles; Meharry Medical College, Nashville, Tenn., 1922; on the staff of the Temple Hospital; treasurer of the Broadway Federal Savings and Loan Association; died Dec. 28, aged 61.

Townsend, Robert Glenn Ⓜ Grayson, Ky.; Tulane University of Louisiana School of Medicine, New Orleans, 1927; member of the American Academy of General Practice; for many years associated with the Stovall Memorial Hospital, where he died Dec. 20, aged 55.

Twohey, Joseph Thomas Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1932; member of the American Academy of General Practice; on the staff of St. Anne's Hospital; veteran of World War II; died Dec. 27, aged 51.

Van Zant, William Emory, Mandeville, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1901; died in St. Tammany Parish Hospital, Covington, Dec. 19, aged 81.

Vastine, Mary Frances Ⓜ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1934; associate professor of radiology at her alma mater; certified by the National Board of Medical Examiners; specialist certified by the American Board of Radiology and the American Board of Otolaryngology; member of the Radiological Society of North America and the American College of Radiology; on the staff of the Hospital of the Woman's Medical College of Pennsylvania; died Dec. 11, aged 52.

Wasson, Valentina Pavlovna Ⓜ New York City; L. R. C. P., London and M. R. C. S., England, 1928; author of "The Chosen Baby" and co-author of "Mushrooms, Russia and History," written in collaboration with her husband, R. Gordon Wasson; attending pediatrician at New York Infirmary; died Dec. 31, aged 57.

Webb, Carol Castor Ⓜ Pensacola, Fla.; born in Albany, Ohio, March 31, 1895; Ohio State University College of Medicine, Columbus, 1918; honorary fellow of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past-president of the Escambia County Medical Society; past-vice-president of the Frisco Railroad Medical Association; became local and later division surgeon of the Frisco Railroad and at the time of his retirement after 25 years' service was one of its consulting surgeons; veteran of World War I; in 1934 elected a director of the First Bank and Trust Company and served up to the time of his retirement; on the honorary staff of the Sacred Heart, Baptist, and Escambia General hospitals; past-president of the Kiwanis Club; died Dec. 29, aged 63.

Weber, Robert Cecil, Muncie, Ind.; Indiana University School of Medicine, Indianapolis, 1942; staff physician at the Veterans Administration Hospital in Marion, where he died Nov. 30, aged 40.

Wentz, John Wesley Ⓜ Pataskala, Ohio; Starling-Ohio Medical College, Columbus, 1910; for many years president of the school board; served on the staffs of the St. Ann's, Mercy, and St. Anthony hospitals, and the Grant Hospital, where he died Dec. 31, aged 73.

White, William Allen Jr. Ⓜ Boston; Harvard Medical School, Boston, 1921; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; assistant professor of clinical surgery at the Boston university School of Medicine; member and president of the staff of the Boston City Hospital; on the staffs of Faulkner Hospital, and New England Hospital; died in Milton Dec. 28, aged 62.

Williams, John Franklin Ⓜ Marion, Va.; Medical College of Virginia, Richmond, 1942; on the staff of the Southwestern State Hospital; died in the Lee Memorial Hospital Dec. 25, aged 58.

Williams, Percy Herbert Ⓜ New York City; Columbia University College of Physicians and Surgeons, New York City, 1901; fellow of the American College of Surgeons; served overseas during World War I; for many years associated with the Lenox Hill and Lincoln hospitals; died Dec. 31, aged 83.

Willson, Harry Leigh Ⓜ Idaho Falls, Idaho; University of Pennsylvania School of Medicine, Philadelphia, 1914; past-president of the Idaho Falls District Medical Society; associated with the Idaho Falls Latter-Day Saints' Hospital and the Sacred Heart Hospital; served as president of the Idaho Falls Rotary Club; died Dec. 29, aged 69.

Wood, T. Kenneth, Williamsport, Pa.; Medico-Chirurgical College of Philadelphia, 1903; for many years practiced in Muncy, where he was one of the founders of the Muncy Valley Hospital, where for many years he was president; established the Muncy Historical Society and was its first president; served as editor of the society's historical journal, *Now and Then;* died Dec. 28, aged 81.

Wright, Harrison Garner Ⓜ Bellingham, Wash.; Johns Hopkins University School of Medicine, Baltimore, 1919; served as president of the King County Medical Society; first president of the King County Physicians Service; fellow of the American College of Surgeons; associated with St. Joseph's and St. Luke's hospitals; died Dec. 23, aged 68.

Yankoff, Peter Demetroff, Fort Smith, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1918; died Dec. 25, aged 74.

Young, Samuel Alexander Ⓜ Cleveland; Western Reserve University Medical Department, Cleveland, 1904; past-president of the Southeast Kiwanis Club; on the staff of St. Alexis Hospital, where he died Dec. 30, aged 79.

FOREIGN LETTERS

GERMANY

Federal Drug Act.—The draft of the Federal Drugs and Pharmaceutical Preparations Act was passed by the government of the Federal Republic of Germany. Although the manufacture of pharmaceutical products has increased steadily since the beginning of this century, German law has not provided for any official licensing of pharmaceutical manufacturers. There were also no legal provisions regarding the qualifications of a head of a pharmaceutical manufacturing plant, and no regulations prescribing equipment, working conditions, safety measures, or hygienic control of the workshops. There is, therefore, an urgent need for laws to safeguard the quality of pharmaceutical preparations and the manufacturing process. The new act bans the manufacture and sale of drugs which are injurious to health or which are spoilt or adulterated in any way. This ban also applies to drugs with misleading designations and drugs made up in a manner which may give rise to misinterpretation or misrepresentation. It also prescribes the labeling and description of pharmaceutical products; for example, the mode of application must be given and the active constituents must be stated, using the designations given in the German Pharmacopeia.

The same regulations apply equally to drugs of foreign manufacture. Any application for permission to manufacture pharmaceuticals will be turned down by the authorities concerned if the person in charge of the manufacturing plant is not suitably qualified. Permission will also not be granted if suitable rooms and equipment for the manufacture, testing, and storage of the products are not provided. The head of a pharmaceutical manufacturing plant must have completed his university training as a pharmacist, chemist, physician, dentist, or veterinarian, and must have had at least one year's practical experience in the manufacture of pharmaceuticals.

Special regulations govern the manufacture of serums and vaccines. The following data must be filed with the application for the registration of any products: qualitative and quantitative composition, fields of application with contraindications, form and mode of application, instructions for use, and results of pharmacological tests and trials if the components include substances whose effectiveness is as yet unknown. This registration merely serves to keep a check on the traffic in pharmaceutical products. The question of the actual need for any particular product is not considered; neither is its therapeutic efficacy tested. Judgment on the efficacy of and on the need for a certain product can only be passed after long and careful examination and thorough clinical trials. Such tests and trials by the government would lead to undue delays in registration which might not be in the interests of the patients or the manufacturer. Registration is to be refused if it is evident that the manufacture of the drug would violate the ban on spoilt or adulterated drugs, on drugs made up in a misleading manner, and on products not properly designated and described.

Kallikrein.—On the basis of his experiments on rats, M. M. Forell of Munich concluded that pancreatic kallikrein participates to a great extent in the digestive process. It is secreted with the pancreatic juice into the duodenum and either increases the absorption of foodstuffs by augmenting the blood supply of the intestinal vessels, or has a physiological effect due to its stimulating action on the intestinal contractions during digestion. It was also shown that the formation of kallikrein by the pancreas and the production of the other enzymes depend on the diet. A meat diet increased the formation both of ferments and of the circulatory hormone, while a diet rich in fat caused a reduction in ferments and production of the circulatory hormone. Reduced or absent urinary excretion of kallikrein followed blockage of the pancreatic ducts, but in diabetes produced by alloxan, despite extensive destruction of islet cells, the formation of kallikrein was undiminished. An incretory formation of kallikrein could not therefore be assumed.

In the urine of healthy persons kallikrein is present in an active form. Since patients with renal hypertension and adrenocortical hypofunction excrete little or no kallikrein, E. Werle and R. Vogel of Munich concluded that in these patients kallikrein would be excreted in the form of the pharmacologically ineffective kallikreinogen. By the action of trypsin on the urine they demonstrated that the urine of patients suffering from renal diseases contained kallikreinogen. The amount of kallikreinogen in the urine was always in direct proportion to the amount of protein. This indicated a passage of the renal barrier together with the plasma protein. The kallikrein released behaved chemically like pancreatic kallikrein: it was destroyed by boiling and inactivated by soy bean inhibitor and ovomucoid. Protein-free urines might,

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The items in these letters are contributed by regular correspondents in the various foreign countries.

however, also contain kallikreinogen, as was demonstrated in patients with myeloid leukemia and diabetes. Kallikreinogen was not demonstrable in the urine of healthy persons.

F. Hollwich and A. Wethmar of Frankfort tested the influence of commercially prepared kallikrein on healthy retinal vessels by direct measurement in 80 persons with normal circulation. Kallikrein was administered in active form (20 to 40 units of Padutin), in depot form (40 to 100 units of Depot-Padutin), and in inactivated form in doses of 100 units. The inactivated form was a combination of Padutin with its natural inactivator and in this form it constitutes a depot that can be activated to 95% in the body by slight shifts in pH. After the intravenous injection of Padutin a measurable effect was observed in 15 to 30 minutes. The maximal effect was seen after 60 to 90 minutes; 20 units of Padutin increased the diameter of the arteries by about 8%, while with 40 units the increase was about 12%. The effect lasted three or four hours with the smaller dose and five or six hours with the larger dose. Corresponding to the protracted absorption of kallikrein from the Depot-Padutin, a dilatation of the retinal vessels occurred only after 45 to 60 minutes and maximal dilatation only after 3 hours. The duration of action with 40 units was 6 to 8 hours and with 100 units 10 to 13 hours. The lumen of arteries dilated by 9 and 11% respectively.

A dilatation of the vessels after three or four minutes of 14 to 21% lasting for about eight hours set in after slow intravenous injection of 100 units of inactivated kallikrein. This rapid and long-lasting effect was manifested by the fact that in the combination of Padutin and an inactivator about 5% of the substance was already present in active form, and that the remaining 95% was gradually activated. After intramuscular injection of inactivated kallikrein the effect set in after 30 to 45 minutes, but it was not inferior to the intravenous administration as regards duration and intensity. Comparative examinations with other vasoactive substances revealed that the effect of all forms of kallikrein application set in later, but (with equal or almost equally high maximum values) showed exceptionally long-lasting effects. This demonstration of the vasodilatory effect of kallikrein was in line with the numerous clinical observations on the therapeutic value of Padutin and Depot-Padutin as seen in circulatory disorders of the arteries of the retina due to spasm or thickening of the wall, in disturbed blood supply of the optic nerves, in senile macular degeneration, and in myopic macular degeneration.

The effect of kallikrein on the peripheral blood supply, which so far was almost exclusively tested on the vessels of the skin in man, was also examined on the musculature by G. Golenhofen and H. Hensel of Marburg. With their new methods, which permitted separate determination of the blood supply of the muscles and the skin, they observed that, through intravenous administration of 10 units of Padutin and 100 units of inactivated kallikrein, an increased blood supply of the muscles was effected in practically all patients. With Padutin this was sometimes about 100% and with inactivated kallikrein up to 200% of the values obtained when resting. An increased blood supply of the skin of the extremities was not seen with the two substances. Only the facial skin showed an increased blood supply and was reddened, with Padutin more than with inactivated kallikrein. The effect which in all cases subsided within a few minutes after a single injection was markedly longer with inactivated kallikrein than with Padutin. Measurement of blood pressure revealed a fall of the average pressure by about 15% for a maximum period of three minutes. At the same time the increase in the pulse rate was 40% on the average and lasted four or five minutes.

Intra-arterial recording of the blood pressure showed that the increased blood supply caused by Padutin was due to a genuine vasodilatation and not to an enhanced pressure-passive supply, but the rise in pulse rate must also be interpreted as a sign of an increased blood supply due to vasodilatation. The trials were carried out on 22 young, healthy persons in 111 single tests, and care was taken that the same room temperature was maintained in all tests and that the patients were in a relaxed position. As the drugs to be tested were slowly infused intravenously in physiological saline solution outside the field of vision of the persons, any possible psychic influencing factor was excluded. During the trial the blood supply of the muscles of the calves and forearm was recorded with the aid of a heat-conducting probe. The blood supply of the skin was measured with a heat-conducting measuring instrument on the ball of the thumb, the sole, or the cheeks.

INDIA

Adrenal Cortical Hypofunction and Amebiasis.—Kasliwal and Mathur (*Journal of the Indian Medical Association,* vol. 31, Dec. 16, 1958) observed that in some patients with chronic amebiasis such clinical features of chronic adrenal insufficiency as asthenia, hyperpigmentation of the skin and mucous membranes, hypotension, and loss of weight were present. They therefore performed tests to assess adrenal cortical function in such patients to find out whether they had adrenal cortical hypofunction. Nine patients with chronic amebiasis diagnosed clinically and by the presence of Entameba histolytica in the stools were thus studied. Cysts of E. histolytica were found in six, trophozoites in one, and two had cysts of both E. histolytica and Entameba coli. All of them had some clinical evidence of chronic adrenal cortical insufficiency such as hyperpigmentation and asthenia. Healthy adults on whom the same tests were made served as controls. The age of these patients varied between 17 and 45 years, and the duration of illness between three months and nine years. The systolic blood pressure ranged between 80 and 104 mm. Hg and the diastolic pressure between 58 and 70 mm. Hg.

All showed hyperpigmentation of the skin and four had hyperpigmentation of the skin and mucous membranes. Two had marked asthenia and four had anemia. Hypoproteinemia and edema were present in all. One patient had hypochlorhydria, another achlorhydria, and one who had a pain resembling duodenal ulcer showed isochlorhydria. Three patients had such mental symptoms as inability to concentrate, insomnia, and marked fatigability. Three had such symptoms of hypogonadism as loss of libido and impotence in men and amenorrhea in women. Low values for serum sodium were obtained in eight patients and high values for serum potassium were obtained in seven. Mild absolute eosinophilia was present in two patients four hours after injection of 0.3 ml. of epinephrine; the eosinophil count fell by more than 50% in three patients and the percentage reduction in the other six was between 28.5 and 40. The urinary 17-ketosteroids ranged between 4.4 and 11.4 mg. in 24 hours in men and 3.1 and 4.7 mg. in women. Seven had a low urinary excretion of 17-ketosteroids and in two it was within normal limits. All these patients improved clinically after antiamebic and symptomatic treatment without any specific therapy for adrenal insufficiency. The exact cause for such insufficiency is not known, but chronic stress imposed by the various manifestations of chronic amebiasis or associated liver damage may be responsible.

Conference on Occupational Health.—Guide lines for the development of the occupational health services in southeastern Asia, made necessary by the increased speed of industrialization, were laid down in the conclusions reached at a southeastern Asia conference in Calcutta. The conference, jointly sponsored by the World Health Organization and the International Labor Organization, recommended that occupational health services be paid for by the employers but the provision of community health services covering workers and their families should be a governmental responsibility. Until community health services are fully developed, occupational health services should provide a certain measure of preventive and curative service, the extent of this being determined by local needs and resources.

These services should cover nonoccupational as well as occupational diseases. Institutes of occupational health should be developed to provide service, research, training, and technical information. Use should also be made of professional organizations in the field of occupational health. The training of physicians in industrial medicine should be given to the medical undergraduate, the physician entering the industrial health field, and the physician desiring to specialize in this subject. The training of industrial nurses and other auxiliary personnel is urgently needed. Persons trained in first aid should be available in every industrial undertaking, and regular courses in first aid should be given by the industrial physician. In establishing occupational health services it is not possible to exclude either legislation or education. Teamwork is a prime necessity in dealing with occupational health problems.

Prostatic Hypertrophy.—B. B. Ohri and co-workers (*Journal of the Indian Medical Association,* vol. 31, Dec. 16, 1958) studied 100 consecutive cases of senile enlargement of the prostate. All were subjected to the Freyer's method of suprapubic prostatectomy. Most of them sought medical attention because of acute retention of urine and were first treated with an indwelling catheter. Those without retention or who had retention with overflow were not catheterized. The series was divided into those whose bladder infection was mild (23), moderate (54), and severe (23). All were given 500,000 units of penicillin and 1 Gm. of streptomycin except those with severe infection who received 2 nitrofurantoin tablets, three times a day for four days. Most of this group had infection with Proteus vulgaris and Pseudomonas aeruginosa. Of the whole series 73 had acute retention. Those with a blood urea above 50 mg. per 100 cc. or with severe infection were treated with an indwelling catheter. Those who had severe urethritis or gross infection of the bladder and those whose blood urea level remained high in spite of the indwelling catheter (26) were subjected to a two-stage operation; 42 suffered from malnutrition and poor general health. The time spent in draining their bladders by an indwelling catheter or suprapubic cystostomy was used to improve their general condition.

The wound after operation usually healed in about two weeks. A bougie (size 9 to 12) was passed through the urethra on the ninth postoperative day as a routine. This prevented the formation of strictures in all but one patient who had a stone in the bladder. All patients received antibiotics postoperatively and nitrofurantoin was given to those with severe infection with P. vulgaris or Ps. aeruginosa. On discharge 42 had mild infection and others were free of infection. Postoperative hemorrhage occurred in four and two of them died. Of the 26 who had a two-stage operation, 4 died, 2 of complications of blood transfusion. The average stay in hospital was 22.3 days. Vasectomy was not done routinely. Gross wound infection after operation occurred in five patients but was treated successfully with nitrofurantoin.

however, also contain kallikreinogen, as was demonstrated in patients with myeloid leukemia and diabetes. Kallikreinogen was not demonstrable in the urine of healthy persons.

F. Hollwich and A. Wethmar of Frankfort tested the influence of commercially prepared kallikrein on healthy retinal vessels by direct measurement in 80 persons with normal circulation. Kallikrein was administered in active form (20 to 40 units of Padutin), in depot form (40 to 100 units of Depot-Padutin), and in inactivated form in doses of 100 units. The inactivated form was a combination of Padutin with its natural inactivator and in this form it constitutes a depot that can be activated to 95% in the body by slight shifts in pH. After the intravenous injection of Padutin a measurable effect was observed in 15 to 30 minutes. The maximal effect was seen after 60 to 90 minutes; 20 units of Padutin increased the diameter of the arteries by about 8%, while with 40 units the increase was about 12%. The effect lasted three or four hours with the smaller dose and five or six hours with the larger dose. Corresponding to the protracted absorption of kallikrein from the Depot-Padutin, a dilatation of the retinal vessels occurred only after 45 to 60 minutes and maximal dilatation only after 3 hours. The duration of action with 40 units was 6 to 8 hours and with 100 units 10 to 13 hours. The lumen of arteries dilated by 9 and 11% respectively.

A dilatation of the vessels after three or four minutes of 14 to 21% lasting for about eight hours set in after slow intravenous injection of 100 units of inactivated kallikrein. This rapid and long-lasting effect was manifested by the fact that in the combination of Padutin and an inactivator about 5% of the substance was already present in active form, and that the remaining 95% was gradually activated. After intramuscular injection of inactivated kallikrein the effect set in after 30 to 45 minutes, but it was not inferior to the intravenous administration as regards duration and intensity. Comparative examinations with other vasoactive substances revealed that the effect of all forms of kallikrein application set in later, but (with equal or almost equally high maximum values) showed exceptionally long-lasting effects. This demonstration of the vasodilatory effect of kallikrein was in line with the numerous clinical observations on the therapeutic value of Padutin and Depot-Padutin as seen in circulatory disorders of the arteries of the retina due to spasm or thickening of the wall, in disturbed blood supply of the optic nerves, in senile macular degeneration, and in myopic macular degeneration.

The effect of kallikrein on the peripheral blood supply, which so far was almost exclusively tested on the vessels of the skin in man, was also examined on the musculature by G. Golenhofen and H. Hensel of Marburg. With their new methods, which permitted separate determination of the blood supply of the muscles and the skin, they observed that, through intravenous administration of 10 units of Padutin and 100 units of inactivated kallikrein, an increased blood supply of the muscles was effected in practically all patients. With Padutin this was sometimes about 100% and with inactivated kallikrein up to 200% of the values obtained when resting. An increased blood supply of the skin of the extremities was not seen with the two substances. Only the facial skin showed an increased blood supply and was reddened, with Padutin more than with inactivated kallikrein. The effect which in all cases subsided within a few minutes after a single injection was markedly longer with inactivated kallikrein than with Padutin. Measurement of blood pressure revealed a fall of the average pressure by about 15% for a maximum period of three minutes. At the same time the increase in the pulse rate was 40% on the average and lasted four or five minutes.

Intra-arterial recording of the blood pressure showed that the increased blood supply caused by Padutin was due to a genuine vasodilatation and not to an enhanced pressure-passive supply, but the rise in pulse rate must also be interpreted as a sign of an increased blood supply due to vasodilatation. The trials were carried out on 22 young, healthy persons in 111 single tests, and care was taken that the same room temperature was maintained in all tests and that the patients were in a relaxed position. As the drugs to be tested were slowly infused intravenously in physiological saline solution outside the field of vision of the persons, any possible psychic influencing factor was excluded. During the trial the blood supply of the muscles of the calves and forearm was recorded with the aid of a heat-conducting probe. The blood supply of the skin was measured with a heat-conducting measuring instrument on the ball of the thumb, the sole, or the cheeks.

INDIA

Adrenal Cortical Hypofunction and Amebiasis.—Kasliwal and Mathur (*Journal of the Indian Medical Association,* vol. 31, Dec. 16, 1958) observed that in some patients with chronic amebiasis such clinical features of chronic adrenal insufficiency as asthenia, hyperpigmentation of the skin and mucous membranes, hypotension, and loss of weight were present. They therefore performed tests to assess adrenal cortical function in such patients to find out whether they had adrenal cortical hypofunction. Nine patients with chronic amebiasis diagnosed clinically and by the presence of Entameba histolytica in the stools were thus studied. Cysts of E. histolytica were found in six, trophozoites in one, and two had cysts of both E. histolytica and Entameba coli. All of them had some clinical evidence of chronic adrenal cortical insufficiency such as hyperpigmentation and asthenia. Healthy adults on whom the same tests were made served as controls. The age of these patients varied between 17 and 45 years, and the duration of illness between three months and nine years. The systolic blood pressure ranged between 80 and 104 mm. Hg and the diastolic pressure between 58 and 70 mm. Hg.

All showed hyperpigmentation of the skin and four had hyperpigmentation of the skin and mucous membranes. Two had marked asthenia and four had anemia. Hypoproteinemia and edema were present in all. One patient had hypochlorhydria, another achlorhydria, and one who had a pain resembling duodenal ulcer showed isochlorhydria. Three patients had such mental symptoms as inability to concentrate, insomnia, and marked fatigability. Three had such symptoms of hypogonadism as loss of libido and impotence in men and amenorrhea in women. Low values for serum sodium were obtained in eight patients and high values for serum potassium were obtained in seven. Mild absolute eosinophilia was present in two patients four hours after injection of 0.3 ml. of epinephrine; the eosinophil count fell by more than 50% in three patients and the percentage reduction in the other six was between 28.5 and 40. The urinary 17-ketosteroids ranged between 4.4 and 11.4 mg. in 24 hours in men and 3.1 and 4.7 mg. in women. Seven had a low urinary excretion of 17-ketosteroids and in two it was within normal limits. All these patients improved clinically after antiamebic and symptomatic treatment without any specific therapy for adrenal insufficiency. The exact cause for such insufficiency is not known, but chronic stress imposed by the various manifestations of chronic amebiasis or associated liver damage may be responsible.

Conference on Occupational Health.—Guide lines for the development of the occupational health services in southeastern Asia, made necessary by the increased speed of industrialization, were laid down in the conclusions reached at a southeastern Asia conference in Calcutta. The conference, jointly sponsored by the World Health Organization and the International Labor Organization, recommended that occupational health services be paid for by the employers but the provision of community health services covering workers and their families should be a governmental responsibility. Until community health services are fully developed, occupational health services should provide a certain measure of preventive and curative service, the extent of this being determined by local needs and resources.

These services should cover nonoccupational as well as occupational diseases. Institutes of occupational health should be developed to provide service, research, training, and technical information. Use should also be made of professional organizations in the field of occupational health. The training of physicians in industrial medicine should be given to the medical undergraduate, the physician entering the industrial health field, and the physician desiring to specialize in this subject. The training of industrial nurses and other auxiliary personnel is urgently needed. Persons trained in first aid should be available in every industrial undertaking, and regular courses in first aid should be given by the industrial physician. In establishing occupational health services it is not possible to exclude either legislation or education. Teamwork is a prime necessity in dealing with occupational health problems.

Prostatic Hypertrophy.—B. B. Ohri and co-workers (*Journal of the Indian Medical Association*, vol. 31, Dec. 16, 1958) studied 100 consecutive cases of senile enlargement of the prostate. All were subjected to the Freyer's method of suprapubic prostatectomy. Most of them sought medical attention because of acute retention of urine and were first treated with an indwelling catheter. Those without retention or who had retention with overflow were not catheterized. The series was divided into those whose bladder infection was mild (23), moderate (54), and severe (23). All were given 500,000 units of penicillin and 1 Gm. of streptomycin except those with severe infection who received 2 nitrofurantoin tablets, three times a day for four days. Most of this group had infection with Proteus vulgaris and Pseudomonas aeruginosa. Of the whole series 73 had acute retention. Those with a blood urea above 50 mg. per 100 cc. or with severe infection were treated with an indwelling catheter. Those who had severe urethritis or gross infection of the bladder and those whose blood urea level remained high in spite of the indwelling catheter (26) were subjected to a two-stage operation; 42 suffered from malnutrition and poor general health. The time spent in draining their bladders by an indwelling catheter or suprapubic cystostomy was used to improve their general condition.

The wound after operation usually healed in about two weeks. A bougie (size 9 to 12) was passed through the urethra on the ninth postoperative day as a routine. This prevented the formation of strictures in all but one patient who had a stone in the bladder. All patients received antibiotics postoperatively and nitrofurantoin was given to those with severe infection with P. vulgaris or Ps. aeruginosa. On discharge 42 had mild infection and others were free of infection. Postoperative hemorrhage occurred in four and two of them died. Of the 26 who had a two-stage operation, 4 died, 2 of complications of blood transfusion. The average stay in hospital was 22.3 days. Vasectomy was not done routinely. Gross wound infection after operation occurred in five patients but was treated successfully with nitrofurantoin.

Tuberculous Meningitis in Women.—K. R. Sathe (*Journal of the Association of Medical Women in India*, vol. 46, November, 1958) reported that tuberculous meningitis, mainly a disease of children, is seen more frequently in women than in men. In a series of 27 women with tuberculous meningitis the age of the patients ranged between 12 and 40 years. The antecedent tuberculous lesions were in the lungs in 9, the abdomen in 5, the spine in 3, and in the remaining 10 no antecedent tuberculous lesion could be detected. This may have been due to the fact that these patients were moribund on admission. In five the disease was associated with pregnancy and in nine it manifested itself in the postpartum period. For this reason pregnant women with known tuberculous lesions should be under constant supervision as the occurrence of tuberculous meningitis in them could be prevented by the early use of specific drugs. In this series 15 died. This high mortality was due to the late stage of the disease at the time of admission. Of those who survived seven had relapses. This emphasizes the need for prolonged and skillful after care.

All the patients showed the characteristic changes in the spinal fluid. Greater reliance was placed on the depression in the glucose content than on the chlorides in the diagnosis. Recovery was not considered complete till the glucose level returned to normal. Acid-fast bacilli could be demonstrated in only one patient. Streptomycin was given in doses of 1 Gm. twice a day in the beginning, followed by 1 Gm. daily for one to two months, combined with PAS and isoniazid. Streptomycin was given intrathecally in the early cases but this practice was discontinued because of the pain it caused and the tendency to favor complications. Cortisone was used in only one patient, due to its prohibitive cost.

Hepatic Coma.—B. B. Bhatia and co-workers (*Journal of the Indian Medical Association*, vol. 31, Nov. 16, 1958) found that the number of patients with hepatic coma treated in the last five years was much larger than that treated in the previous five years. During this period, however, a larger number of patients with hepatic cirrhosis and infectious hepatitis applied for admission, and the percentage of hepatic coma associated with these conditions remained the same (about 5% in those patients with cirrhosis of liver and 4% in those with infectious hepatitis). The incidence of hepatic coma in patients with infectious hepatitis was a little higher in this series than in those reported by observers in other countries. This may have been due to delayed treatment and lack of rest in the beginning of the illness which is common here. The authors' series consisted of 58 patients (42 men and 16 women, in 5 of whom the coma was precipitated by pregnancy).

The most common exciting cause of coma in this series was intestinal hemorrhage and the authors recommended that in any patient with cirrhosis of the liver, at the onset of mental symptoms, the stools and vomitus be examined carefully for blood. Other exciting causes were acute infection, administration of ammonium chloride and acetazolamide, high protein diet, and pregnancy. The administration of acetazolamide for the relief of ascites precipitated the onset of coma in two patients. In the group with infectious hepatitis the major precipitating cause was pregnancy. All five pregnant patients were in the third trimester. The occurrence of infectious hepatitis in this period should be regarded as a serious complication. In one patient coma followed physical exhaustion.

Superadded acute infection precipitated coma in all patients with cholangiohepatitis. Treatment therefore consisted in avoidance of physical exertion and prescribing a high-protein diet, ammonium chloride, acetazolamide, urea, meperidine, morphine, and barbiturates. The diet should consist mainly of carbohydrates and proteins. Acute infections and hemorrhagic tendencies should be controlled. Between 1,000 and 1,500 ml. of 25% dextrose solution should be given intravenously every day and one capsule of tetracycline should be given hourly by mouth or in nasal feedings. About 75 Gm. of glutamic acid was given daily but its value was doubtful. The authors do not advocate a completely fat-free diet. The ideal diet for the patient is high in carbohydrate, with average protein and fat content. ACTH and cortisone are probably useful when the coma has supervened on an infectious hepatitis.

Chlorpromazine for Mental Disease.—N. N. Chatterji (*Journal of the Indian Medical Association*, vol. 31, Dec. 1, 1958) treated with chlorpromazine 137 patients who had schizophrenia, 65 who had manic-depressive psychosis, 35 who had obsessions or compulsions, 32 who had hysteria, 25 who had paranoia, 16 who had involutional melancholia, 12 epileptics with mental symptoms, 8 who had an anxiety state, 4 who had dementia, 4 drug addicts, and 4 who had periodic depression. The age of these patients ranged between 15 and 45 years. The usual dosage was 200 mg. daily in divided doses. A Rauwolfia preparation containing lucin-H was also given to those with paranoia, paranoid schizophrenia, and manic excitement. The duration of treatment varied from three to six months. Most patients tolerated the drug well. Toxic symptoms met with in some were severe constipation, diarrhea, jaundice, cutaneous rashes, paralysis agitans-like symptoms, giant urticaria with serous discharge from all the body openings, and fever.

The differential blood count in patients with fever showed neutropenia, eosinophilia, and relative lymphocytosis while the total leukocyte count showed leukopenia. Those who received large doses for a long time suffered from lethargy, weakness, and fatigue. Patients with schizophrenia, manic-depressive psychosis, and involutional melancholia responded well to the drug. Among the schizophrenics the best results were obtained in those with the catatonic variety. The symptoms disappeared within three weeks, and there was no need to give them shock treatments. In paranoid schizophrenics, although no response was obtained with chlorpromazine alone, good results were seen when it was combined with lucin-H, some patients being completely cured and others being able to go back to their social and occupational life in spite of the persistence of minor delusions.

In the paranoiac group, nine were completely cured with this combination. Manic-depressive psychosis showed an excellent response to chlorpromazine. The response was better in the manic phase when it was used in combination with reserpine. The depressed phase of manic-depressive psychoses subsided quickly with chlorpromazine. Results were good in patients with involutional melancholia but not in those with senile dementia. The increased excitability after fits in epilepsy were controlled with chlorpromazine. Among the psychoneurotic group, good response was seen in some patients with hysteria (mutism, aphonia, and fits). Good results were seen in obsessional neurosis. In drug addiction, although none was cured, the withdrawal period was easier with the use of chlorpromazine. Good results were obtained in patients with anxiety neurosis.

UNITED KINGDOM

Hazards for Young Doctors.—The hazards and rewards of different professions were discussed before the Royal Commission on Doctors' and Dentists' Remuneration. British Medical Association representatives said the road before the future hospital consultant was longer and more uncertain than that for men of other callings. The young physician, having completed seven years' undergraduate training, must serve in a hospital for a year as a provisionally registered practitioner and for two years in the armed forces before he will be free to decide on the direction of his career. By then contemporaries in other walks of life would have advanced to a point from which definite career prospects were in sight. Although the training for all professions is longer now than it used to be Dr. S. Wand, chairman of the B. M. A. Council, reminded the Commission that young men in some other fields are able to earn money en route. Invited to compare the young physician and the young barrister Dr. D. P. Stevenson, the association's secretary, said that whether or not the young barrister succeeded was very much in his own hands, but the young doctor might be forced into another branch of the profession outside the hospital field not because he was incapable but because there were no vacancies.

Dr. Gregory Dead.—Dr. J. C. Gregory, chairman of the All-England Lawn Tennis Club, Wimbledon, and a former Davis Cup player, died in the dressing-room of the club on Jan. 10, just after he had finished a doubles match. He was 55 years of age and had been in practice for nearly 25 years. He first represented England in 1926 when, as a member of the Davis Cup team, he played against Spain and France. From 1949 to 1953 he was the non-playing captain of the British Davis Cup team. After giving up the captaincy of the British Davis Cup team Dr. Gregory became vice-chairman of the All-England Club, and was elected chairman in 1955.

Future of the Tuberculosis Service.—The changes which have taken place in the last few years in the field of tuberculosis are the subject of an editorial in the *British Medical Journal* of Jan. 31. Although many beds for pulmonary tuberculosis have been closed because of the more rapid turnover of patients, hospital work has not decreased proportionately. On the other hand, the work of chest clinics may have increased. Since more patients suffer from pulmonary diseases other than tuberculosis, the work is much less routine in character than formerly. Figures obtained from 18 chest clinics showed that in one winter month of 1958 only 22% of new patients were diagnosed as having respiratory tuberculosis while 30% had acute respiratory disease and 27% had chronic respiratory diseases other than tuberculosis.

The Joint Tuberculosis Council strongly endorsed the view that facilities for the management of tuberculosis should be widened to serve patients with other respiratory diseases. This has already been done in many areas. Chest clinics are well able to coordinate inpatient, outpatient, preventive, and social services in the interest of patients with chronic respiratory diseases. They are peculiarly well suited to handle the problems presented by chronic bronchitis and to diagnose and treat bronchial carcinoma.

Perineal Carriage of Staphylococci.—Dr. M. Ridley, lecturer in bacteriology, St. Thomas' Hospital, London (*British Medical Journal*, Jan. 31, 1959) said that the possibility that the perineal region might be a carrier site on which Staphylococcus pyogenes var. aureus could multiply had been suggested but no information was available on the proportion of the population who are perineal carriers, whether they can disperse the organisms into free air, or the relationship between nasal and perineal contamination or carriage. A survey of 50 men showed that

52% had no Staph. pyogenes var. aureus in the nose or on the skin, 26% had this organism in the nose, generally in large numbers, but that the perineal area yielded fewer than 30 colonies from the six sites (total of 300 sites) chosen for examination. A further 12% had much greater degrees of contamination of the perineal area and were heavy nasal carriers as well. The remaining 10% had an equal degree of contamination of the perineal area but no Staph. pyogenes var. aureus in the nose, or at most five colonies. Thus, sufficiently large numbers of Staph. pyogenes var. aureus can be isolated from the perineal area of 22% of men to class them as perineal carriers. Further investigations showed that this state may persist for months in about 14%, that it is not due to fecal contamination alone, that the organisms can multiply in or on the perineal skin, that they may be of a different bacteriophage type from those found in the nose or feces, and that they may be dispersed into free air when the subject exercises in a cubicle.

Cost of Running Hospitals.—The cost of maintaining a patient in a London teaching hospital has risen to an average of $93 a week. This is shown in returns for the year ended March 31, 1958, and published by the Ministry of Health. The comparable figure in provincial teaching hospitals was $90. In nonteaching hospitals of 1 to 50 beds it was $59 and in those of 101 to 300 beds, $66. The average weekly cost in other types of hospital was as follows: chronic disease hospital, $26.50; maternity, $65; mental illness, $18; mental deficiency, $17; tuberculosis, $47; and children's acute disease, $63. Comparisons must be made with caution because of changes in accounting methods introduced in April, 1957. The net inpatient cost per patient at different hospitals averaged as follows: London teaching, $217; provincial teaching, $147; nonteaching, 101 to 300 beds, $130; maternity, $101; children's acute disease, $133.

Reducing Hospital Infections.—The widespread use of antibiotics, lack of facilities for isolating infected patients, and shortage of staff were among the chief causes of hospital infections, according to the report of Lord Cohen's Committee on Staphylococcal Infections in Hospitals. Unfortunately, funds and equipment are not universally available to allow staffs to carry out all recommended precautions (*Lancet*, Jan. 24, 1959). Staphylococcic disease was a major hospital problem before the era of antibiotics. The miraculous effect on it of penicillin, in 1944, was followed within two or three years by the appearance of the first penicillin-resistant strains of staphylococci. Today the drug is useless for most hospital epidemics. The breeding of drug-resistant strains has tended to increase the virulence of the organism and consequently to produce more severe infections. The fact that these are all theoretically avoidable in epidemic form led to the suggestion that penicillin be voluntarily withheld for a trial period of two years.

Lord Cohen's committee suggested that antibiotics such as erythromycin be kept solely for the treatment of infections due to strains resistant to other antibiotics and, except in emergency, should be prescribed only by a senior staff member. Strict observance of aseptic methods, not the use of antibiotics, is now necessary for the elimination of this serious problem. The report recommends extensive regular sterilization of all bedding, ward curtains, and other hospital materials with the suggestion that cotton blankets are more suited to this than woolen ones. The isolation of patients and of staff infected with whitlows and other staphylococcic infections is of paramount importance.

Reply to Attacks on Medical Profession.—Having read a letter from Sir Walter F. Hannay in the *Daily Telegraph* in which he deplored the trade union attitude of the British Medical Association, Prof. Charles Wells replied by means of an open letter in the *Daily Telegraph* of Jan. 22. He emphasized that the B. M. A. has never advanced the idea that physicians should withdraw service from their patients. What the B. M. A. suggested was withdrawal from the National Health Service and the provision to patients of continued medical attention at their own expense, the less affected areas subsidizing the more severely affected areas pending solution of their differences with the Minister of Health. Most trade unions would regard this as major lunacy.

A Cheaper Health Service.—A cheaper alternative to the National Health Service is being worked out by the British Medical Association. It might save the country as much as $840,000,000. The annual cost of the Health Service now exceeds $1,960,000,000 per year. It increases yearly as prices, salaries, and wages rise. The Association's Amending Acts Committee has laid down a series of basic principles which should underlie the new plan. The first is a statement that the preservation of private practice is essential to the development of medicine in this country, and its extension would insure a saving in public funds. The new plan would be financed by the state, the patient, and insurance. Payment by the patient would give him a sense of responsibility. There would be free care for the medically indigent. At present family physicians are paid a fee of $2.52 a year for each patient on their lists up to a maximum of 3,500 with an addition of $1.68 for each patient between the numbers of 501 and 1,500, bringing the fee for these patients to $4.20. This method of payment would be discontinued. Doctors would be paid a fee for each service rendered.

Concerning the possibility of abuse Dr. A. V. Russell, chairman of the Amending Acts Committee, said that there was some over-attendance in the early days of the Australian service, but this had been stopped by the profession itself. The principle of payment on a tripartite basis would free the service from the risk of political interference and enable the responsibility for its administration to be vested in a body on which the three contributing parties could be represented. Other principles laid down by the committee were (1) freedom of the physician, under safeguards, to prescribe whatever medicines he thought best; (2) restoration of the personal patient-physician relationship; (3) academic and professional freedom; and (4) avoidance of operating the health service in watertight sectional compartments.

Before any scheme is finally approved the draft must be considered by several interested committees. Endorsement by the Association's annual representative meeting would be necessary before such a plan became Association policy. The extent to which the state, the patient, and insurance, respectively, would pay for the cheaper alternative to the NHS has not yet been worked out. The only certainty is that the patient would contribute more than he does today through National Insurance, but he would stand to gain as a taxpayer.

The British Medical Association.—The Council of the British Medical Association has been forced to review its balance sheet. It has found that the existing dues for each ordinary members of $17.60 per year is insufficient to balance the budget. The prewar rate was $5.90. The Council decided, against strong opposition, to recommend to the representative body in July that the dues for 1960 be raised to $26.45. The principal reasons for the increase are inflation, the increase in the cost of the production of the *British Medical Journal*, the additional cost of the annual clinical meeting, further developments in regional offices, and the cost of fighting the Association's battles. Some believe that such a large increase will induce some members not to renew their membership, or to deter others from joining. Some suggest a means test whereby doctors in some of the lower income groups would pay a reduced charge while those in the surtax group would be expected to pay more. Many members fail to appreciate what the Association has achieved for them in its efforts to improve the conditions of service.

Poliomyelitis Vaccination.—Of the 6,250,000 people aged 15 to 26 who become eligible in the autumn for vaccination against poliomyelitis only 250,000 have been injected, and 96,000 of these have received only one dose. Ministry of Health officials and local health officers are disappointed and puzzled by the lack of response. Special efforts, such as evening clinics and injections at place of work, have been made to reach these young people. Local health authorities are starting a renewed drive. More special clinics and sessions at places of work will be arranged, and posters will urge young people to take advantage of the scheme. The acceptance rate for children up to the age of 15 is mounting, but both it and the response from expectant mothers must be improved.

Lung Cancer and Tobacco.—The Feb. 7 issue of the *British Medical Journal* contains three articles on lung cancer and tobacco. One of these, by R. Doll and co-workers, shows a definite relationship between the death rate from lung cancer and the length of discarded cigarette butts. In spite of the well-known difficulties of international statistical comparisons they found a distinct relationship in 16 countries between the reported cigarette consumption in 1930 and deaths from lung cancer in the period 1952-1954. Striking exceptions were Japan and the United States, which had a relatively high cigarette consumption but a relatively low incidence of lung cancer. In the United States one explanation may lie in the larger cigarette butt that the smoker discards. A comparison of cigarette butts specially collected and measured in Britain with similar data recently reported from the United States gives an average length of 30.9 mm. in the latter country against 18.7 mm. in the former. Of the cigarette butts in the British sample 67% were less than 20 mm. in length, and only 2.5% were as long as 30 mm. In the American sample less than 10% were smoked down to 20 mm., and 50% were discarded with 30 mm. or more still unsmoked. Such a large national difference in habits might greatly influence the national exposure to any carcinogen in cigarette smoke.

An article by I. T. T. Higgins of the Pneumonoconiosis Research Unit of the Medical Research Council discussed the relationship between tobacco smoking, respiratory symptoms, and ventilatory capacity in a series of 734 men between the ages of 25 and 64 who were randomly selected from urban and rural populations. A questionnaire was used to record respiratory symptoms and smoking habits. A clear relationship between smoking and persistent cough and sputum was invariably found, and smokers also tended to record more chest illness, wheezing, breathlessness, and chronic bronchitis than nonsmokers. Nonsmokers had a higher mean maximum breathing capacity than smokers; the best estimate of the difference, allowing for the size of the various groups studied, being 9 liters a minute. There was, however, no significant downward trend with increasing tobacco consumption among the smokers.

CORRESPONDENCE

THERAPY IN THE ANEMIAS

To the Editor:—In the June 7, 1958, issue of The Journal, page 735, an article entitled "Current Status of Therapy in Anemias," by Lichtman, states that parenterally administered iron, for example, in the form of an iron-dextran complex (Imferon) in great excesses over a long period of time will produce "exogenous hemochromatosis." Since parenteral therapy with properly calculated dosage of iron-dextran complex should be discontinued when a hematological response has been obtained, as well as when this type of therapy fails or the patient eventually becomes anemic, iron-storage diseases, i. e., hemosiderosis or hemochromatosis, should not occur under these circumstances, because the possibility of iron overload is eliminated. The subject of iron-overload has been discussed in a textbook, "Iron in Clinical Medicine" (edited by Wallerstein and Mettier, Berkeley, University of California Press, 1958). The question of whether hemosiderosis progresses to hemochromatosis has been answered both affirmatively and negatively. Much of the difference of opinion is a result of the different clinicopathological criteria used in defining hemosiderosis, hemochromatosis, and cirrhosis. From the studies of Baggenstoss, Weir, Kark, and myself—based on autopsy data from 35 patients with primary hemochromatosis, 7 with secondary hemochromatosis, and 21 with hemosiderosis and data from 10 living patients (9 with primary hemochromatosis, and 1 with secondary hemochromatosis)—we were able to establish definite clinical and pathological criteria mandatory in defining these conditions.

The evidence that iron per se does not produce hemochromatosis is summarized as follows: 1. The administration of iron, intravenously, orally, or in the form of blood transfusions in human beings, causes transfusional hemosiderosis but not hemochromatosis. 2. The administration of iron, orally or parenterally or in combination with cirrhotogenic diets, over long periods to experimental animals produces only hemosiderosis. 3. The amount of iron administered to patients through blood transfusions does not correlate with the degree of cirrhosis or hepatic, myocardial, or pancreatic fibrosis. 4. Oral Fe^{59} absorption studies, serial liver biopsies, serum iron and iron-binding capacity determinations, and evaluation of genetic traits of patients with hemochromatosis differ from those with hemosiderosis, which is actually only a pathological condition.

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ACROMIOCLAVICULAR SEPARATIONS AND DISCUSSIONS OF PAPERS

To the Editor:—The report on suspension cast for acromioclavicular separations and clavicular fractures, published in The Journal (169:672-675 [Feb. 14] 1959) and presented at the A. M. A. meeting in San Francisco last June, leaves much to be desired. The paper gives the impression that many patients have been treated this way and that the results were good. However, what we saw when the paper was given was most inconclusive. It appeared that the acromioclavicular joints were still separated in the cases shown and that the suspension cast gave no better results than did a posterior figure-of-eight support in bilateral clavicular fractures. It is unfortunate that the discussion of this paper was not also presented in The Journal. In it these points were clearly brought out and doubt was cast on the value of this method of treatment. Many papers published in various journals lose their value when the discussion at the time of presentation is not also reproduced. Frequently the discussion points up the good and bad points of the method presented and entirely changes one's concept of whether or not it is worthy of a trial.

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F. B. I. ITEMS IN THE JOURNAL

To the Editor:—In The Journal (169:640 [Feb. 7] 1959) is a letter from Dr. Guttmacher, of Baltimore, in which he criticizes the occasional acts of cooperation of The Journal with the F. B. I. I hope that there will be a continuation of appropriate aid to our law enforcement officers. I am sure that most physicians in the United States feel the same way.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Breach of Warranty.—This was an action for damages against the defendant psychiatrist. From a summary judgment for the defendant in the trial court, the plaintiff appealed to the United States court of appeals for the District of Columbia.

Because of the plaintiff's condition, the defendant recommended the administration of a series of electric shock treatments. Prior to giving them, contended the plaintiff, the defendant advised that the treatments were "perfectly safe," and she said she submitted to the treatments in reliance on such assurance. When she regained consciousness after one of the treatments, the plaintiff found that she had a fractured left arm.

The defendant denied making the statement attributed to him by the plaintiff. In a deposition, however, he said that the plaintiff's fracture was caused by the convulsive seizure which ensued as a result of the electric shock treatment and that in his practice this had occurred on seven or eight other occasions.

Doubtless, said the court, a physician's statement that he would cure a disease could seldom if ever be regarded as a warranty. But that is not this case. The statement attributed to the defendant, that shock treatments are "perfectly safe," contains less of prediction and more of present fact. We think this statement, if the defendant made it and did not qualify it in any way, might properly be found to be a warranty.

The summary judgment in favor of the defendant was therefore reversed. *Johnston v. Rodis*, 251 F (2) 917 (1958).

Malpractice: Delay in Using Lipiodol Dye X-Ray Technique with Lipiodol.—This was an action for damages for pain and suffering caused by the alleged negligence of the defendant surgeon. From a judgment for the defendant, the plaintiff appealed to the court of appeals of Maryland.

The patient, deceased wife of the plaintiff, was suffering from an advanced stage of cancer of the descending colon when she was referred by her own physician to the defendant for surgery. He found that a large cancer in the upper part of the descending colon had gone through all three coats of the intestine and had become attached to the back. He felt that complete removal of the tumorous mass would afford the best chance of preventing the spread of the cancer and of survival of the patient. In spite of the difficulty he removed a large portion of the colon, together with the large tumor, all in one piece and then joined together the two remaining sections of the intestine. After the operation the patient continued to have a fever for six weeks for which a variety of treatments were used including drugs, blood transfusions, and drainage operations. After the second drainage operation consultants were called in to attempt to locate the continuing difficulty. The consultants concluded "that there was still a collection of pus somewhere in the abdominal cavity that required drainage." It was suggested that two types of x-rays be taken, chest x-rays to determine the level of the diaphragm, and instillation of lipiodol dye to determine whether or not there was a tract that led to a pus pocket. The suggestion of injecting the dye in the fistulous area was adopted, the tract where the pus had accumulated showed up clearly, and an effective drainage operation was performed.

The gravamen of the plaintiff's charge was that the defendant delayed unduly in the use of the dye technique to locate accurately the pus accumulations.

There is a presumption, said the court, that a doctor has performed his medical duties with the requisite care and skill. The burden of proof is on the plaintiff to show both a lack of the requisite skill or care on the part of the doctor and that such want of skill and care was a direct cause of the injury; and if proof of either of these elements is wanting the case is not a proper one for submission to the jury. The plaintiff's main difficulty was the lack of affirmative proof of negligence on the part of the defendant.

We think, concluded the court, that the plaintiff has failed to meet the burden of presenting evidence which would support a finding of negligence. Though it might be inferred that if he had used lipiodol dye sooner the patient would have fared better, we do not think that the plaintiff has produced proof that the defendant was guilty of negligence in failing to use it sooner and in seeking to locate and drain the pus pockets by other means. He was clearly successful in locating a pus pocket on his first drainage incision, and that fact alone seems to prevent an inference that a dye injection was a necessary means of discovering the location of pus. Nor do we think that there is any such common knowledge of the use and efficacy of the dye method as to warrant us in holding that the jury might find, without supporting expert testimony, that the surgeon was wanting in reasonable diligence, skill, and learning because he failed to use this dye test in addition to others at an earlier stage of postoperative care of the patient.

Accordingly the judgment of the trial court in favor of the defendant physician was affirmed. *Lane v. Calvert*, 138 A (2) 902 (Md., 1958).

MISCELLANY

FOREIGN MEDICAL GRADUATES

A PROGRESS REPORT

T. Stewart Hamilton, Hartford, Conn.

The number of graduates of foreign medical schools taking the examination of the Educational Council for Foreign Medical Graduates is increasing by almost geometric progression and will reach an expected peak in 1959. In March, 1958, 298 physicians wrote the first examination; 844 wrote the September, 1958, examination; and some 2,300 have applied for February, 1959. It is important that we assess the status and the potential of this program as we plan for the future.

The ECFMG was formally established in 1957, after preliminary discussion and planning over the previous decade.[1] Its primary objective was to promote opportunities in the United States for advanced studies in medicine, to the end that the level of medical care might be raised throughout the world. Its primary concern was to safeguard the health care and welfare of the American public; therefore, it sought to determine that foreign medical graduates participating in patient-care educational programs in the United States had reached a level of educational attainment comparable to that of graduates of medical schools in the United States and Canada. ECFMG is sponsored by the American Medical Association, American Hospital Association, Association of American Medical Colleges, and Federation of State Medical Boards of the United States. Its trustees, composed of representatives of the sponsoring organizations and the public, have developed and implemented a plan for evaluation of credentials and administration of a qualifying examination. At the same time they have sought and obtained funds from the Kellogg and Rockefeller Foundations to initiate the program and engaged Dr. Dean F. Smiley as the executive director.

In March, 1958, the first examination was given to 298 physicians in centers in the United States and Canada. These graduates of foreign medical schools had already had from 1 to more than 20 years' experience with medicine in the United States. Questions were taken from those tested and used by the National Board of Medical Examiners. The questions were selected as being least likely to confuse those whose command of English was somewhat limited. Of these 298 physicians only 151 (51%) attained a passing grade of 75 or higher,[2] a disappointing result.

At the American Hospital Association convention in September concern was expressed that the new examination would greatly reduce the numbers of interns coming to the United States. Concern was also expressed that agreement by the National Intern Matching Program to accept certified foreign medical graduates for matching along with graduates of United States and Canadian schools would further deplete the intern supply available to hospitals now relying on these men and women to fill their quotas. These questions were voiced both at the Council on Professional Practice Review Committee meeting on Aug. 17, 1958, and later before the House of Delegates. Although no formal action was taken, the record of these proceedings included the suggestion of one delegate that "(a) The American Hospital Association . . . take steps to defer if at all possible, the inclusion of foreign medical graduates into the intern matching program until the program has been further evaluated and (b) to examine and test the present mechanism in view of the high percentage of failures."[2]

This seemed to relieve the administrators' minds, at least for the moment, since a program on the subject of the foreign medical graduate held later in the convention attracted a relatively small audience and evoked few comments or criticisms. It seemed that most delegates, while worrying about the possible implications of the program for their own institutions, recognized the need for such a controlled plan.

The ECFMG Examinations Committee reviewed the results of the March examination with great care and, noting that many who took it complained of its length, recommended that the number of questions be reduced and the time for its completion be extended. The question of lowering the passing grade from 75 to 70 was discussed at length. Decision against such a step was made on the ground that if it were taken the ECFMG could no longer state that the certified physician had reached a level of educational attainment comparable with that of a graduate of a United States school.

Dr. John P. Hubbard toured the world for the ECFMG during the summer of 1958 and set up 27 examination stations in Central and South America and overseas. On Sept. 23, 1958, 844 graduates of foreign medical schools whose credentials had been studied and approved wrote the new examinations, 707 in the United States and Canada and 137 in foreign centers.[3] Of those writing in U. S. stations 52.4% passed, which indicates that changing the examinations to reduce the number of questions and extend the time for their completion had little if any effect, for 51% had passed the first examination. A new and serious problem arose when the scores of those writing the examination overseas were compared with those of United States examinees. This is demonstrated graphically in the chart. While those writing in the United States did

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Director of the Hartford Hospital.

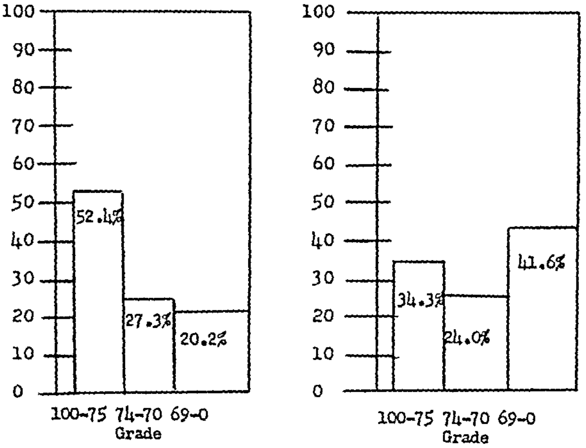
rather better than the March examinees, scarcely more than one-third of those writing in foreign stations attained a passing grade.

It was at once obvious to the Examinations Committee that to limit the number of certified foreign medical graduates from without the United States and Canada to barely more than one-third of those taking the examination would be serious indeed. It was obvious as well that, in comparing the results of the two groups, students benefited greatly from what they learned in the United States. For these reasons it was decided that a new category be established, called Temporary Certification. Temporary certificates, valid for two years' postgraduate training in the United States, will be given to examinees who attain scores of 70-75. By the end of the two years the graduate will be expected to have written and passed the certifying examination. The new category of Temporary Certification will entitle the holder to apply for any approved internship in the United States and to be matched through the National Intern Matching Program.

The decision to issue temporary certificates to those whose scores were within five percentage points of a passing grade was approved by the trustees as an expedient measure in the face of the unexpectedly poor showing of those who wrote the examination outside the United States. By its issue the percentage of examinees receiving either permanent or temporary certification was raised to 76.2. Of those writing in the United States 79.7% attained grades of 70 or higher while of those writing in foreign centers 58.3% attained such scores. Of the 844 who wrote the September examination 226 (26.7%) will receive temporary certificates. If they plan to take more than two years' postgraduate training in the United States it will be necessary for them to retake and pass the ECFMG examinations during that period. The two years is deemed necessary to give the graduate time to improve his knowledge, reapply, and rewrite the examination.

What of future examinations? As noted above, 2,300 graduates of foreign medical schools have applied to write in February, 1959; it is expected that at least an equal number will apply for the September, 1959, and February, 1960, examinations. After July 1, 1960, the date when all graduates holding internship and residency appointments will be expected to have qualified, the number of applicants should fall to between 2,000 and 3,000 per year. These will be graduates of foreign medical schools who are seeking appointments for the first time together with those holding temporary certification and others who apply to rewrite the examination. Examinations will be given as at present both in the United States and in foreign stations. Cost of the administration will be borne by both the applicants and the hospitals appointing them, the charge being $50 to the applicant and $75 to the hospital. Those eligible to apply will be graduates (and in some instances students in their last year) of schools listed in the World Health Organization World Directory of Medical Schools. Applications will be screened at the Council's headquarters, 1710 Orrington Ave., Evanston, Ill. Although actual scores and results of examinees by school or by nationality will be kept confidential lists of those certified will be made available to state medical boards and other authorized bodies.

While the program is scarcely under way and has had to face the usual problems of any new organization it already shows promise of the accomplishment of its twofold purpose: improving educational opportunities for graduates of foreign medical schools and insuring an adequate quality of care for patients. State boards of medical examiners in 16 states, for example, have already agreed to accept ECFMG permanent certificates as evidence for admission of a foreign-trained physician to their licensing examinations. It is expected that ECFMG permanent certificates will soon come to be regarded around the world as evidence that the holder has attained a level of medical competence equivalent to that of a graduate of a United States or Canadian school. In order to succeed the ECFMG will need the continued support of its sponsoring agencies and their membership. If it succeeds it can be a vital factor in the improvement of world medicine and world health.



Results of examinations taken by graduates of foreign medical schools at United States stations (*left*) and at foreign stations (*right*).

This article is being published simultaneously in the April 1, 1959, issue of *Hospitals.*

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MEDICAL LITERATURE A

INTERNAL MEDICINE

Serum Triglycerides in Coronary Artery Disease. M. J. Albrink and E. B. Man. A. M. A. Arch. Int. Med. 103:4-8 (Jan.) 1959 [Chicago].

Lipids are transported in serum as constituents of 3 major classes of compounds: cholesterol and its esters, phospholipids, and triglycerides or neutral fat. Most investigations in recent years have centered about the notion that serum cholesterol plays a causative role in the development of coronary artery disease. Although triglycerides rather than cholesterol are chiefly responsible for turbidity of serum and constitute an important fraction of β-lipoproteins, the quantitative estimation of triglycerides has been largely neglected in studies of serum lipids in coronary artery disease. The present research was undertaken to observe the interrelation of the 3 major serum lipid fractions. The subjects were 100 patients with a history of myocardial infarction. The group included 82 men and 18 women, ranging in age from 21 to 78 years, the greatest number being in their 50's. Control subjects included healthy medical students, industrial workers, and hospital patients without vascular disease and without known metabolic disorders.

Elevations of serum triglycerides above 5.5 mEq. per liter (about 160 mg. per 100 cc.) occurred in only 5% of normal young adults, in at most 30% of normal men over 50, and, if the effects of acute illness were excluded, in 85 to 90% of patients with coronary artery disease. The authors believe that few, if any, other lipid measurements which have been reported effect such a clear-cut separation between normal and coronary subjects. The observations reported suggest that an error in the metabolism of triglycerides is the lipid abnormality operative in coronary artery disease. It may be that other findings commonly reported in this disease, such as increased cholesterol, increased low-density lipoproteins rich in triglycerides, and prolonged and intensified alimentary lipemia, are secondary to decreased efficiency of resulting accumulation It is tempting to speculate o these findings in relation to the e of the heart, particularly in the light dence that fat is an important source of normal myocardium, that triglycerides are over with great rapidity by heart tissue, and lipoprotein lipase occurs in high concentration in myocardial tissue.

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Several illustrating case histories are presented, and the author discusses various aspects of the postmyocardial infarction syndrome. It differs from the common "pericarditis epistenocardica" by longer duration of fever and chest pain and by relapses of fever and pleuropericardial pain; the pericardial friction rub lasts longer or occurs later than usual; there is pericardial effusion which is often associated with pleurisy and pneumonitis; recurr are common. The exudate may be he The postmyocardial infarction syndro distinguished from the 2 conditions been mistaken: (1) from extensi infarction, by the pleuro pain and the absence of addi electrocardiogram, and (2) fr

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Improvement resulted in 23 of the 25 episodes of coma. Eleven of the 22 patients died, but in 9 of these 11 some improvement was noted before death. Eighteen patients received protein from the beginning of therapy with neomycin, and of these 7 lived and 11 died, but some improvement was noted before death in 9 of the latter. Four patients received no dietary protein, and all survived, but of these, 3 had bleeding and thus had protein within the intestinal tract. A decrease in the level of blood ammonia was observed during therapy in 16 of the 18 patients in whom it was determined. Of those whose ammonia levels fell 8 lived and 8 died, with all the patients showing some improvement prior to the final outcome. Death occurred in both patients in whom the ammonia level did not fall during neomycin therapy, and neither patient exhibited improvement. No significant difference in survival rate was observed between patients receiving more than 25 Gm. of protein and those receiving less than 25 Gm. An unfavorable prognosis in these patients was found to be associated with increasing depth of coma after therapy was initiated and with the presence of jaundice.

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Remission of the Hematological and Clinical Symptoms in Acute Leukemia After Treatment with Prednisone and 6-Mercaptopurine. P. Longo. Policlinico (sez. prat.) 65:1639-1648 (Oct. 27) 1958 (In Italian) [Rome].

Complete remission of the hematological and clinical symptoms was obtained by treating a 17-year-old youth with acute leukemia with prednisone and 6-mercaptopurine. The first symptoms of the disease occurred in the patient one year before admission to the hospital. Upon admission the patient received several 200-cc. transfusions of fresh whole blood and treatment with analeptic drugs and vitamins. Prednisone and 6-mercaptopurine were given 4 days later. Prednisone was administered first in a dose of 30 mg. per day and later in a dose of 80 mg. per day, which was continued for 22 days; 6-mercaptopurine was administered in a dose of 150 mg. every 24 hours, which was continued throughout the period the patient remained in the hospital and was reduced to 100 mg. per day after discharge from the hospital. Three additional 200-cc. blood transfusions were made before discharge from the hospital.

The condition of the patient was critical during the first 15 days he spent in the hospital. A gradual improvement could be observed after this period. The patient started to take some food, and the temperature tended to decrease. Later a marked improvement of the objective and subjective conditions followed day by day. Swelling of the lymph nodes became reduced and almost disappeared. The contour of the spleen and of the liver became normal. The infection of the mouth and throat healed, and no trace was left of it. The color of the patient became normal, and the body weight, which was 57.3 kg. (126 lb.) on admission, went up to 65 kg. (143 lb.). Fever disappeared completely 6 weeks after admission, at which time the appetite increased markedly and the digestive process was normal. The patient was discharged from the hospital after 16 weeks and, when seen 1 month later, was found to be in good general condition. The hematological examination at this time gave normal results.

Armchair Treatment with and Without Anticoagulants in Cardiac Infarction. S. Helander. Acta. med. scandinav. 162:351-359 (no. 5) 1958 (In English) [Stockholm].

The author reports on 307 patients with cardiac infarction, who were admitted within 3 days of onset and received armchair treatment, with and without anticoagulants, at the Karolinska Sjukhuset in Stockholm between 1952 and 1956. The aim of the armchair treatment was to relieve the heart muscle. The patients were divided into 3 groups according to the severity of their condition. Group 3 included the mild cases; group 2 included patients with the usual clinical symptoms of cardiac infarction, with fever, raised erythrocyte sedimentation rate, and leukocytosis; and group 1 included the most severely ill patients, with additional manifestations of shock and a fall in blood pressure. Fifteen of the 307 patients died within 12 hours after admission and are not included. Of the remaining 292 patients, 112 were treated in an armchair and were given anticoagulants (10% of these died): 100 were treated in an armchair without anticoagulants (15% of these died); and 80 were treated with bed rest and anticoagulants (26% of these died). It is significant that 6% of the patients from group 2 who received armchair treatment with anticoagulants and 16% of the patients from the same group who received armchair treatment without anticoagulants died, whereas of the patients of group 2 who received treatment with anticoagulants and bed rest 22% died. Most of the patients who died showed ominous prognostic signs, such as arrhythmia in cardiac failure or heart block, and about half of them had had a previous attack of cardiac infarction, as postmortem examination had revealed. Of the patients treated in an armchair, there were 14 who had had a previous attack of infarction among the 25 patients who died. Twelve patients of the armchair group had a septal infarction, against 9 of 21 patients treated with bed rest. The frequency of embolic complications was negligible in all groups and could hardly have had any effect on the mortality.

An analysis of the immediate causes of death in cardiac infarction seems to suggest that armchair treatment lessens the burden placed on the heart muscle and diminishes the risk of occurrence of pulmonary edema. Embolic complications do not seem to have played any role in determining the difference in mortality rates between those treated with anticoagulants and those who did not receive anticoagulants. Armchair treatment seems to be a good prophylaxis against thromboembolic complications in patients with cardiac infarction.

Syndromes of Thyroid Hyperfunction in Old Age: Clinical Study. C. de Nogales Quevedo and M. Santaló Rovira. Med. Clín. 31:83-105 (Aug.) 1958 (In Spanish) [Barcelona, Spain].

Three hundred patients with hyperthyroidism were observed at the hospital of the University of Barcelona; of these patients 20 (17 women and 3 men) were between the ages of 50 and 70 years. The older patients complained of repeated bouts of hyperthyroidism, with cardiac decompensation and periods of either nervousness or depression. Psychic trauma was the only, or the predominant, causal factor of hyperthyroidism in more than half of them. On hospitalization, all these patients reported considerable loss of weight during the past few months, and they all had tachycardia and tremor. Hyperthyroidism was of either the apathetic (Lahey's) type or the type of exophthalmic goiter. Hyperthyroidism of the apathetic type had appeared in 10 women several years after the menopause. The cardiovascular disease was severe, 5 of the patients having atrial fibrillation with complete arrhythmia. Exophthalmos and goiter either were not present or were very mild. The constant psychic feature was depression. Hyperthroidism of the type of exophthalmic goiter appeared in 7 women immediately or shortly after the menopause. The ocular, thyroid, and cardiovascular symptoms were the same as those observed in patients whose exophthalmic goiter had developed at a younger age. The psychic feature was constant nervous tension.

The treatment of these older patients with hyperthyroidism consisted of the administration of methylthiouracil in daily doses which ranged from 0.15 to 0.3 Gm. This dosage was given in 3 or 4 fractional doses for several days during early therapy. Then the patients were placed on maintenance therapy in which the dosage was individually determined and was given for 3 or 4 months until complete remission was obtained (100% satisfactory results were reported in all these cases). Remission has lasted for several years since discontinuation of the treatment in all the patients but 2. These 2 patients had a recurrence 7 months and 1 year, respectively, after the first remission, but a second complete remission, which has lasted several months, was obtained once more from the administration of methylthiouracil. The authors conclude that thyrotoxic goiter in older patients is a clear indication for treatment with methylthiouracil; the drug is well tolerated. Surgical treatment of hyperthyroidism in this age group is indicated only in cases of nodular goiter or when canceration of the goiter is threatening. Seven representative cases are reported.

A Comparative Study of the Effect of Transfusion of Fresh and Preserved Whole Blood on Bleeding in Patients with Acute Leukemia. E. J. Freireich, P. J. Schmidt, M. A. Schneiderman and E. Frei. New England J. Med. 260:6-11 (Jan. 1) 1959 [Boston].

Gross bleeding in patients with acute leukemia is closely related to thrombocytopenia. With the development of plastic and other nonwettable surfaces, the transfusion of viable platelets that circulate for 5 to 7 days was demonstrated, but because of difficulties involved in platelet transfusion, it cannot be employed as a standard therapeutic procedure. For these reasons, freshly drawn whole blood, collected over nonwettable surfaces, has been utilized for the treatment of thrombopenic bleeding in patients with acute leukemia. Preliminary clinical observations of the effect of fresh whole-blood transfusion on hemorrhage in acute leukemia indicated definite benefit in only an occasional patient. Moreover, the extreme irregularity of hemorrhage in these patients, as well as the frequently transient nature of the hemostatic effect, often made clinical judgement of effectiveness extremely difficult. In view of the extra time, effort, and expense involved in utilizing fresh blood for transfusion, it seemed necessary to evaluate quantitatively the effect of this treatment.

The present study was designed as a controlled, comparative blind study, with banked whole blood as a control material. It was found that fresh blood collected in disodium ethylenediaminetetraacetate alters hemorrhage in patients with acute leukemia more frequently than bank blood collected in acid citrate dextrose and stored at 5 C for 2 to 9 days. Favorable responses to fresh blood were observed in 10 of 14 bleeding episodes. Platelet levels after fresh-blood transfusion were significantly higher than those after bank-blood transfusion. However, all levels were well below the platelet level ordinarily associated with absence of hemorrhage (50,000 per cubic millimeter). The platelet levels after fresh-blood transfusion were not significantly different for those showing a clinical effect and those showing none.

SURGERY

An Analysis of the Pathologic Anatomy of Pulmonary Arteriovenous Aneurysms with Particular Reference to the Applicability of Local Excision. L. H. Bosher, D. A. Blake and B. R. Byrd. Surgery 45:91-104 (Jan.) 1959 [St. Louis].

The authors analyzed the gross pathological anatomy of pulmonary arteriovenous aneurysms in 252 patients whose cases were collected from the world literature and in 98 patients whose cases have not been previously reported. The anatomic distribution of pulmonary arteriovenous aneurysms in the 350 patients showed a wide variability, ranging from multiple, diffuse, pulmonary telangiectasia to a single large aneurysm. Twelve cases are recorded in which a systemic artery joined the aneurysm. About 64% of the patients had single lesions, and in 75% the disease was unilateral. Angiography should be performed preoperatively in all patients to detect fistulas which are not visualized on plain chest roentgenograms. Of the 350 patients, 239 were operated on, and on 19 of these, bilateral resections were performed. There were 13 operative deaths. Seventeen patients, less than 10 years old, were operated on, and all but one of these obtained good results.

A technique for performing local excision of arteriovenous aneurysms in a bloodless field is reemphasized, and it is estimated that this can be employed in at least 50% of all cases, in preference to segmental resection or lobectomy. To illustrate the applicability of this technique, the case of a

39-year-old man with a large subpleural aneurysmal sac on the underface of the anterior segment of the left upper lobe is reported. The technique was utilized as follows: After occlusion of the main pulmonary artery and superior pulmonary vein together with the main bronchus, the sac was entered and the vascular orifices were observed, two of arterial origin, 6 mm. in diameter each, and one of venous origin, 1 cm. in diameter. The two arteries were ligated individually close to the base of the sac, but the large vein was dissected some distance proximally where it joined a vein from the anterior segment. The postoperative course of this patient was uneventful. Reexamination one year later revealed that he had gained 20 lb. (9.1 kg.) and that the previously noticed shortness of breath on exertion was no longer present. It is urged that surgeons should report any cases of late recurrence which might elucidate further the problem of latent small pulmonary arteriovenous fistulas.

Clinicopathologic Observations on the Fate of Arterial Freeze-Dried Homografts. A. W. Humphries, W. A. Hawk, V. G. de Wolfe and F. A. Le Fevre. Surgery 45:59-71 (Jan.) 1959 [St. Louis].

The authors report on 525 patients with occlusive and aneurysmal disease, who were operated on and in whom arterial freeze-dried homografts were placed in the abdomen and in the lower extremity. In 31 patients the grafts were initially unsuccessful because of inadequate runoff. There was a total of 56 deaths; 4 of these were caused by technical failure of an inadequate proximal anastomosis in patients with aneurysm; of 10 patients who died as a result of failure of the homograft itself, 6 had local infections with resultant rupture of the graft, 2 died of erosion of the homograft as it pulsated against the cut end of the patient's own calcified vessel, and 2 died of rupture of a saccular aneurysm. Causes associated with major surgery, but not specifically with a graft, were responsible for the other 42 deaths. These included deaths due to myocardial infarction, rhythmic changes in the heart, usually ventricular fibrillation, and cerebral anoxia. A total of 438 patients thus were available for follow-up studies. Of these, 70 have incurred some incident in their postoperative course that has resulted in the loss of distal pulses and a presumed failure of the graft. In 368 patients the grafts remained successful for periods ranging up to 4½ years.

Of the 70 patients in whom late graft shutdown has occurred, 15 had aortoiliac and 55 had femoropopliteal grafts. All these patients had occlusive disease. Five had grafts which were lost through primary wound infections in the leg. These, combined with the 6 deaths due to infection, make a total of 11 infections (or 2%). In the presence of infection with associated proteolytic digestion of the homograft, the only safe procedure is to remove the graft, tie off the patient's own vessels, and abandon the project. Thirty of the late graft shutdowns were regrafted. Two of them were initially unsuccessful, a second late shutdown occurred in 2, and the remaining 26 regrafts are still potent and functioning. Most of the late graft shutdowns occurred in the femoropopliteal area due to the smaller caliber of the vessel, and most of the shutdowns occurred within the first year. Pathological findings in 33 grafts, 30 of which were obtained from regrafting and 3 from patients whose deaths occurred late, were as follows. Arteriosclerosis occurred in 7 of the grafts removed; multiple aneurysmal dilatation occurred in 1 case; arteriosclerotic aneurysm occurred in 1 femoral graft; saccular aneurysm developed in 4 grafts; 1 dissection occurred within a graft; and there were 11 instances of rupture due to infection.

Long-standing good results may be expected in those patients with aneurysm who survive the surgical intervention. One may also expect a certain acceptable percentage of late shutdowns in patients with occlusive disease, not necessarily of clinical importance, more in femoropopliteal than in aortoiliac grafts, which is in direct proportion to the size of the vessel, to degree of "activity" of disease, and undoubtedly to other as yet unknown factors. However, the longer a graft remains functional, the better the chances are that it will continue to remain functional.

Congenital Pulmonary Arteriovenous Fistula: Report of a Case and Review of the Literature. A. G. Fletcher Jr., K. Banerjee, T. Takaro and W. M. Bond. Indian J. Surg. 20:416-422 (Oct.) 1958 (In English) [Madras].

The authors report on a 28-year-old man with pulmonary arteriovenous fistula for which he was operated on at the Wanless Tuberculosis Sanatorium in Miraj, India. There was a history of repeated attacks of pain in the lower chest on the left, but there was no history of cough, expectoration, or fever. Chest roentgenograms revealed a homogeneous circumscribed area of increased density in the left lower lung field toward the periphery. On fluoroscopy the lesion was shown to be anterior in position, probably in the lingula of the upper lobe. It was considered to be a circumscribed caseonecrotic focus or tuberculoma. The patient was given antimicrobial therapy for 6 months, on which he gained 17 lb. (7.7 kg.) in weight, but the lesion did not respond to therapy. A left-sided thoracotomy was performed, and on exposing the lung a soft, rounded, pulsating mass located just beneath the visceral pleura was found in the superior portion of the lingular segment. A strong thrill was palpable on slight compression of the lesion, which appeared to be a pulmonary arteriovenous fistula. Lingulectomy was performed to remove the lesion. The patient made an uneventful recovery and was free of symptoms when last seen one year after the operation. He apparently was the first patient operated on for pulmonary arteriovenous fistula and reported on in India. The cases of 40 patients with pulmonary arteriovenous fistula, who were operated on, were collected from the literature. There was only one postoperative death.

Pulmonary arteriovenous fistula is a relatively uncommon congenital defect with a hereditary tendency. The typical clinical picture is that of cyanosis and clubbing in a patient with a normal heart and a lung lesion revealed by chest roentgenogram. Polycythemia may be severe, but in some patients it may be absent or minimal. The diagnosis may be confirmed by laminography or angiocardiography. Dangerous complications reported by other workers were hemoptysis, hemothorax, brain abscess, bacterial endarteritis, and cerebral thrombosis. The treatment of choice is surgical resection of the involved portion of the lung after carefully checking for multiple lesions.

Intra-Aortic Blood Transfusion. V. S. Ermakov. Khirurgiya 34:23-27 (no. 11) 1958 (In Russian) [Moscow].

The author reports on 10 cases in which transfusion of blood into the abdominal aorta was employed in grave surgical shock and in blood loss. A good and stable effect was seen in 7 patients who recovered; an effect of short duration was obtained in 2 patients. The author's observations show that the intra-aortic transfusion of blood is a powerful therapeutic measure which may be employed in prophylaxis and in combating severe shock. The rise in arterial blood pressure and an improvement in the cardiac activity and respiration appeared directly after the injection of the first portions of blood. The total amount of blood injected in shock was 70 to 140 ml., while in shock combined with blood loss it was 250 to 300 ml. The author suggests a special method for intra-aortic blood transfusion, which enables one to control the aortic blood pressure and, consequently, to determine the required amount of blood for the achievement of the effect.

Spasm: A Preliminary Clinical Report on a Nondestructive Method for the Relief of So-Called "Mass-Reflex" Spasm. D. Munro and E. L. Spatz. New England J. Med. 260:1-6 (Jan. 1) 1959 [Boston].

This paper deals only with the so-called mass-reflex spasm. This occurs solely in connection with injuries of the spinal cord between the 3rd cervical and 1st sacral segments. Of the 3 characteristics of the mass-reflex spasm, the first is an excessive, self-propagating, maximal motor response to a minimal sensory stimulus. Muscular overresponse takes the form of a strong, spastic, slowly released movement of the various parts of the limb at the individual joints. The motion may be either pure flexor, pure extensor, alternate, or mixed. If the spasm causes pure flexion, the great toe is first dorsiflexed, followed by fanning of the other toes and dorsiflexion of the ankle. This activity is rapidly propagated without further external stimulus to the flexors of the knee, then to the adductors of the thigh, the flexors of the thigh, and the paraspinal and psoas muscular groups with flexion at the waist; if the cord injury is high enough, there is a spread to the abdominal muscles, as well as the adductors and flexors of the arm, forearm, and hand.

If not corrected, and as the various muscle groups are involved one by one, the position of the legs and body becomes firmly fixed in either flexion, if the spasm started as pure flexor spasm, or extension, if it started as pure extensor spasm. Mixed flexor-extensor spasm will present a confusing picture of limb fixation, but the basic self-provocative nature, progression, and distribution will be present in any case. The second characteristic of the mass-reflex spasm is its tendency to form a vicious circle as the result of repeated sensory stimuli, which originate in the area of muscle and tendon contractions and which, in turn, produce more muscle responses out of which arise, in their turn, more motor-producing sensory stimuli. The third characteristic is the semi-isolated reaction, which involves in its own vicious circle the bladder, the external urethral sphincter, the rectum, and the anal canal.

A previously unreported method designed to eliminate the mass-reflex spasm in patients with spinal-cord injuries is reported. This method has been based upon the hypothesis that such spasm differs from other spasms in that, in its pure form, it is self-propagating from the periphery, progresses centrally, and has circular form. The urinary bladder, the external urethral sphincter, and the intestine-emptying mechanism are all adversely affected by the mass-reflex spasm and may remain so after the skeletal-muscle spasm is abolished. This visceral spasm is also self-propagating and circular in form. Permanent abolition of spasm of the detrusor and external urethral sphincter can be brought about by properly placed procaine and, rarely, by alcohol injections of the sciatic roots through the sacral foramens in the former condition and by injection of procaine into the internal pudic nerves in the latter condition. Destructive permanent denervations, whether surgical or chemical, of the parasympathetic and somatic nerve supply to the bladder and the external urethral sphincter, as well as destruction of the urethra by punch operation, are not necessary and are practically always contraindicated. Previous abolition of skeletal mass-reflex spasm is an essential prerequisite if this therapy is to succeed. Selective

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Injection with procaine, or its derivatives, of the sciatic nerve in the thigh and of the ulnar, median, and radial nerves in the arms shows promise of further success in the control of spasm associated with partially injured spinal cords even in quadriplegic patients. The sciatic nerves should be exposed for injection through a posterior upper-thigh approach at the first injection. The procaine solution should be injected under direct vision into the nerve trunk. The epineural sheath must not be incised. Silver clips should be so placed as to indicate the place and plane of future injections, which should then be done with fluoroscopic guidance of the injecting needle. The ulnar, median, and radial nerves should all be exposed for injection under direct vision at the level in the arm where they surround the brachial artery. The physiological implications of the control of abnormal postural reflex activity, as demonstrated in the cases reported, warrant further investigation.

Symptomatic Myelolipoma of the Adrenal Gland: Report of a Case and Review of the Literature. L. Parsons Jr. and J. E. Thompson. New England J. Med. 260:12-15 (Jan. 1) 1959 [Boston].

Myelolipoma of the adrenal is rare, and so far has been described only as an incidental finding at autopsy. The case reported here is of interest, because the authors believe it to be the first recorded case in which a myelolipoma reached a large enough size to produce symptoms necessitating operative removal. The patient was a 51-year-old woman, hospitalized in October, 1956, with a 2-month history of malaise, anorexia, and poorly localized discomfort in the upper abdomen. These symptoms were increasing. In the month before admission there had been occasional nausea and vomiting, as well as a 5.4-kg. (12-lb.) weight loss. The discomfort was unrelated to foods. Intermittent headaches were a complaint of long standing. In the right upper quadrant of the abdomen there was a large, rounded mass extending 5 fingerbreadths below the costal margin in the midclavicular line. The mass was slightly tender; it moved with respiration and with manipulation.

At exploratory operation, the colon was seen to overlie a large retroperitoneal mass. The retroperitoneal space was entered, and an ovoid tumor was seen lying on the vena cava just above the right kidney. Mobilization of the tumor was readily performed, except at its upper pole where it was contiguous with a thinned-out rim of adrenal tissue. The patient made an uneventful recovery, with relief of the symptoms. There has been no evidence of recurrence. The specimen was a large, oval mass, 25 cm. long, 13 cm. wide, and 12 cm. thick. It weighed 1,250 Gm. Sectioning of the growth revealed adipose tissue, the structure and organization of which were similar to those seen in lipomas in general. The adipose tissue was traversed by bundles of fibrous tissue. The purplish areas observed on gross examination represented, variously, adipose tissue, markedly congested sinusoids, fresh and old hemorrhages, and occasional clusters of lymphocytes, as well as bone-marrow tissue with hematopoietic elements. The peripheral orange-yellow tissue described on gross examination was adrenocortical tissue beneath a fibrous capsule. No adrenal medulla was seen in the many sections examined.

The Use of Intravenous Pituitrin in Treatment of Bleeding Esophageal Varices. S. I. Schwartz, H. W. Bales, G. L. Emerson and E. B. Mahoney. Surgery 45:72-80 (Jan.) 1959 [St. Louis].

The authors treated 11 patients with acutely bleeding esophageal varices by intravenous administration of a commercial posterior pituitary preparation (Surgical Pituitrin) or a commercial preparation of vasopressin injection (Pitressin). The estimated blood loss before the institution of therapy varied between 250 and 1,000 cc. Ten of the 11 patients had alcoholic cirrhosis. A Levin nasogastric tube or an uninflated Sengstaken-Blakemore tube was inserted in 9 of the patients in order to maintain a constant gastric suction and thus decrease regurgitation into the esophagus of gastric fluid. Twenty clinical units of Surgical Pituitrin or Pitressin, usually diluted with 200 cc. of 5% dextrose in distilled water, were administered over a half-hour period, and the nasogastric tube irrigated at half-hour intervals. Rapid infusion is necessitated by the tachyphylactic property of the drugs. Therapy can be repeated at 4-hour intervals if there is evidence of continued or recurrent bleeding. In the group of 9 patients, 25 distinct episodes of acute bleeding were so treated, with prompt control 22 times. The gastric aspirate cleared 5 to 20 minutes after the completion of the intravenous administration of Surgical Pituitrin or Pitressin. In 2 patients in whom transthoracic esophagotomy resulted in brisk "arterial"-type bleeding, which obscured the surgical field and made identification of the individual varices extremely difficult, 20 units of Surgical Pituitrin were administered over a period of 3 minutes, with a dramatic reduction in the intensity of the bleeding, thus making the individual varices more apparent for suture.

Surgical Pituitrin and Pitressin are worthwhile additions to the therapy of bleeding varices. Direct portal venous pressure measurements in patients with esophageal varices have shown that intravenously administered Surgical Pituitrin results in a rapid and marked lowering of portal pressure, equivalent to the level achieved by portacaval shunt. The drugs have proved effective in the control of acutely bleeding esophageal varices and have been helpful in facilitating transesophageal ligation of bleeding varices. It is recommended that an intravenous regimen with Surgical Pituitrin or Pitressin be given an initial trial in the control of bleeding in view of the distinct advantages over balloon tamponade.

Anastomosis Between the Subclavian Artery and the Aorta in Surgical Treatment for Coarctation of the Aorta. T. De Nunno and R. Gentilli. Minerva cardioangiol. 6:513-518 (Oct.) 1958 (In Italian) [Turin, Italy].

A successful anastomosis between the subclavian artery and the aorta, according to the technique of Blalock, was performed on 4 patients with coarctation of the aorta, aged between 16 and 30 years. The considerable length of the constricted segment of the aorta in 3 patients and a laceration of the upper segment of the aorta which occurred during operation made unfeasible an end-to-end anastomosis between the 2 segments of the aorta. Interruption of the subclavian artery did not cause trophic disturbances in the contiguous upper extremity because of an abundant collateral blood supply. The blood supply of the lower extremities was also adequate, being confirmed by preoperative and postoperative blood pressure recordings. The arterial blood pressure was about 210/90 mm. Hg in the upper left extremity and about 100/90 mm. Hg in the lower extremity before the operation. These values approached each other closer in these patients after the operation, being approximately 140/80 mm. Hg in the upper extremities and the same or slightly lower in the lower extremities 10 days after the operation. The patients were well 2 months after the operation. Vertigo, headache, and head pulsation disappeared in those instances in which they were present before the operation, and blood pressure in the lower and upper extremities showed insignificant changes from previous recordings. Anastomosis between the subclavian artery and the aorta thus permitted the reestablishment in this series of patients of a circulatory condition close to the normal pattern.

Development of Primary Pyloric Hypertrophy in Adults in Relation to the Structure and Function of the Pyloric Canal. S. C. Skoryna, H. S. Dolan and A. Gley. Surg. Gynec. & Obst. 108:83-92 (Jan.) 1959 [Chicago].

Adults with pyloric hypertrophy exhibit ill-defined but somewhat ulcer-like symptoms. The variable symptomatology and difficulty in distinguishing with absolute certainty between benign pyloric stenosis and malignant tumors of this region account for the fact that a proportion of these cases will continue to be undiagnosed before surgical exploration. The authors call particular attention to the relationship of the development of primary pyloric hypertrophy in adults to the structure and function of the pyloric canal. The histories of 6 adults with pyloric hypertrophy, who were studied in the department of surgery of St. Mary's Hospital and of the Royal Victoria Hospital, Montreal, are presented. Their ages ranged from 31 to 61 years. All were operated on, and the diagnosis of pyloric hypertrophy was confirmed by histopathological studies. The structure of the pyloric canal is described on the basis of anatomic findings. The structure of the circular musculature of the pyloric canal appears to be of primary significance in this region. It consists of circular muscle fibers forming a distal (pyloric) loop and a proximal (intermediate) loop enclosing an area of circular fibers which are parallel on the greater gastric curvature side and by convergence form a muscle torus on the lesser curvature. It is concluded that the development of the primary pyloric hypertrophy in adults is related to this structure of the circular muscle layer of the pyloric canal. The physiological evidence for the existence of a pyloric canal mechanism rather than of a pyloric sphincter is discussed.

Primary pyloric hypertrophy in adults is divided into (1) a focal form (torus hypertrophy), (2) a diffuse form associated with proximal lesions, and (3) a diffuse form without other lesions. It is suggested that a congenital neuromuscular dysfunction of the pyloric canal mechanism forms a common basis for both the infantile and the adult pyloric hypertrophy. The relative incidence of each form appears to be determined by the extent of the normal regression in the circular musculature of the pyloric canal during early infancy and by the action of secondary factors during adult life.

Perforated Gastric-Duodenal Ulcers and Their Treatment. M. Pastori. Minerva chir. 13:1263-1267 (Nov. 15) 1958 (In Italian) [Turin, Italy].

The author reports on 119 patients with peptic ulcer who had received surgical treatment since 1937. Duodenal ulcer was present in two-thirds of the patients. The average age of the patients was 35 years. The series included only 4 female patients. The greatest incidence of the disease was observed in spring and in autumn. Perforation was treated by gastroenterostomy in 32 patients (mortality rate, 25%), by resection in 7 (mortality rate, 28%), and by simple suture in 80 (mortality rate, 12.5%). Gastroenterostomy had been used earlier but recently gave way to other surgical methods. There were no deaths among 32 patients treated recently by a simple suture. For this reason the author has selected simple suture, complemented by continual aspiration before and after the operation, as the procedure of choice in the treatment of perforated ulcer. Gastric resection, though, remains the most efficacious surgical procedure for treatment of ulcerous disease in the course of its normal development.

The Management of Massive Hemorrhage from Diverticular Disease of the Colon. C. M. Earley Jr. Surg. Gynec. & Obst. 108:49-60 (Jan.) 1959 [Chicago].

This report reviews observations on 23 patients with massive bleeding associated with diverticular disease of the colon, who were treated at the Medical College of Virginia Hospitals, Richmond, from January, 1952, to August, 1957. They represented 4.5% of the 486 patients diagnosed during this time as having diverticulosis. No attempt was made to study patients with occult or minimal bleeding. Rather, this article is concerned with bleeding sufficiently massive to be noticed by the patient and to cause him to seek medical attention. Other possible causes for the bleeding must be ruled out. The ages of the 23 patients ranged from 44 to 81 years, the average age being 65 years. There were 14 women and 9 men. Hypertensive cardiovascular disease was present in 13. One patient had 4 hospital admissions with massive bleeding; 5 others had 2 admissions each. Data on all 23 patients are tabulated, and 8 especially interesting case histories are described in detail.

The initial care is conservative, with supportive therapy including adequate blood replacement. Most patients will respond to it and cease to bleed quite as suddenly as they began. The average volume of blood administered to the 16 patients managed conservatively was 1,000 cc. per hospital admission. The 7 patients requiring surgical treatment for control of hemorrhage received an average of 6,000 cc. of blood each. A review of the literature revealed a total of 23 patients who were treated surgically in order to control hemorrhage from colonic diverticular disease. Most of these procedures were performed as emergencies, and most of the patients were over 60 years old. At operation, all of the colon containing diverticula should be resected, unless the actual bleeding point can be identified. In a bleeding patient too critically ill to tolerate resection or colectomy, proximal ileostomy or colostomy may be helpful, although there is no certainty that the bleeding will stop after this procedure.

Fibrinolysis and Hypofibrinogenemia: Three Cases. P. H. Sørensen. Ugesk. laeger 120:1669-1674 (Dec. 11) 1958 (In Danish) [Copenhagen].

Fibrinolysis is thought to originate by the introduction of lysokinase into the blood stream, by the release of tissue activators, or by inactivation of inhibitors. Hypofibrinogenemia may be a result of the fibrinolysis, which can cause a fibrinogen consumption increased beyond the production ability of the liver. In the same way a powerful stimulation of the coagulation process on release of tissue thromboplastin can cause hypofibrinogenemia. Finally, there may be so strong an effect on the liver that reduced liver function and hypofibrinogenemia result. The first of the cases reported was that of a woman, aged 60 years, with cancer of the stomach and extensive metastases. Profuse bleeding from the urinary tract developed. Hypofibrinogenemia and fibrinolysis were established. In spite of blood transfusion and administration of plasma and fibrinogen, the patient died 5 days after the beginning of the bleeding. In a multipara, aged 33 years, admitted because of premature separation of the placenta, there were shock, fibrinolysis, and slight hypofibrinogenemia. Treatment with dextran, blood, fibrinogen, and pitupartin was applied; the patient recovered. In the third instance, in a man, aged 60 years, with metastasizing cancer of the prostate, afibrinogenemia and fibrinolysis leading to cutaneous and cerebral hemorrhage developed shortly before death.

Debricin—Clinical Experiences with a New Proteolytic Enzyme in Surgical Wounds. J. F. Connell Jr., L. R. M. Del Guercio and L. M. Rousselot. Surg. Gynec. & Obst. 108:93-99 (Jan.) 1959 [Chicago].

During the past 7 years the burn research group at St. Vincent's Hospital, New York, has been evaluating many enzymatic materials for wound débridement. Debricin proved to be the material that best fulfilled the requirements of an ideal wound débridement agent. This enzymatic agent was developed from ficin in the sap of the fig tree. While highly active against fully denatured protein, the material is only partially active on marginal necrotic tissues. There has been no evidence of systemic toxicity and very little evidence of wound maceration. The powdered material comes mixed with a buffer, and it is activated by mixing the enzyme into a special jelly base. The dry material is stable indefinitely, and, after mixing, the refrigerated material is stable for at least 7 days. The buffered enzyme is most active at pH 5.4. Dilution by strong acid or base producing organisms or antibiotics will tend to be inhibitory.

The material must be applied so that the enzyme-substrate contact is kept at a maximum, and reapplied at 12-to-24-hour intervals to remove inhibitory by-products. There is little difficulty in applying the enzyme to postoperative wounds, deep ulcers, fistulas, sinus tracts, or chest cavities, but flat surface areas, such as shallow ulcers or burns, will tax the surgeon's ingenuity. The best method for the flat surface lesions is to spread the enzyme in a jelly base thickly over the area, cover this with a petrolatum gauze or polyvinyl sheet, and overlay the whole with a thick, absorbent pad. A second method of treating the flat surface eschar is to apply the enzyme as a wet dressing, suspending the buffered material in 100 cc. of isotonic sodium chloride solution and instilling it every 3 to 5 hours through rubber catheters tunneled in an absorbent pad overlying the eschar. The outer surface of this pad should be covered by a polyvinyl sheet to limit evaporation.

The main purpose of using the enzyme is to clean a wound of necrotic tissue elements and to thin out thick exudative collections. The authors used Debricin in 139 patients with a variety of surgical lesions. They found that there is rapid, complete débridement when the enzyme is properly used on various types of ulcerations, deep burns, sinus tracts, and wound infections. Debricin used topically is nontoxic. Antibiotics should be utilized during the course of therapy. The enzyme improves the conditions for healing by its cleansing activity. Its use should be followed by the appropriate surgical procedure to obtain wound closure when indicated. Further studies on local enzyme-antibiotic combinations are in progress.

PEDIATRICS

Esophageal Stricture from Accidental Ingestion of Clinitest Tablets. C. Zimmerman. A. M. A. J. Dis. Child. 97:101-103 (Jan.) 1959 [Chicago].

The author presents the history of a 3½-year-old girl, who was admitted to the Bronx Municipal Hospital Center, New York, on Aug. 6, 1957. The patient began vomiting intermittently 3 weeks prior to admission, about 1 week after a visit to her maternal grandmother, a diabetic. This vomiting progressed, as did anorexia and weight loss, until admission. The vomitus consisted of partially digested food. Physical examination was negative. On the third hospital day the grandmother volunteered the information that the patient had swallowed a Clinitest tablet which was used in urine testing. On the fourth hospital day an esophagogram revealed a stricture of the esophagus just above the level of the carina. Esophagoscopy showed the stricture, and a tube gastrostomy was done. When esophagography was repeated later, it showed complete obstruction at the stricture site. After unsuccessful attempts at dilatation, the stenotic segment was resected, and an end-to-end anastomosis was performed. Four weeks after surgery the patient was eating strained bulky foods.

Four other cases of esophageal stricture caused by Clinitest tablets were found in the literature. Three of these involved children; one also had a complete stricture. An esophagogram will confirm the clinical impression of esophageal stenosis or stricture. If the patient has contact with a diabetic and no etiology is apparent, ingestion of Clinitest should be considered. This tablet can cause a partial or complete stricture of the upper esophagus because of the action of the lye constituent. The copper sulfate content may play a secondary role.

The Infant of the Diabetic Mother. S. S. Gellis and D. Y-Yung Hsia. A. M. A. J. Dis. Child. 97:1-41 (Jan.) 1959 [Chicago].

Despite its large size and apparent maturity the infant of the diabetic mother behaves much like a premature infant and is very frail. About a third of such infants die either in utero or in association with respiratory distress during the early neonatal period. In the 3 decades since the discovery of insulin the problems of the diabetic mother and her infant have received much attention. The authors evaluate the work previously done in this field, and they add observations made on 934 pregnancies of diabetic women in the Joslin Clinic, Boston, between 1940 and 1956. The women were seen in the clinic during pregnancy and were subsequently delivered at the Faulkner Hospital (1940-1950) and the Boston Lying-in Hospital (1950-1956). All the patients were under the care of a team consisting of an internist, 2 obstetricians, an anesthetist, and a pediatrician.

Pregnancy failures were several times commoner in women with diabetes mellitus than in healthy women. This excessive loss was limited mostly to the period after the 28th week of gestation. Comparison of mortality figures showed no significant decrease in the fetal mortality in recent years. Experience and teamwork in therapy seemed to influence the ultimate outcome of such pregnancies. Two maternal factors appeared to influence the fetal mortality: (1) severity of maternal disease and (2) good diabetic control. While there is evidence that diabetic women have a hormonal imbalance during pregnancy and that this is frequently associated with the death of the fetus, there is no proof that female sex hormones either correct this defect or significantly reduce the fetal mortality rate.

Infants of diabetic mothers should be delivered between the 35th and the 36th week of gestation. This prevents the high mortality rate associated with prematurity if delivery takes place too early and the marked increase of stillbirth if delivery takes place closer to term. There is no evidence that the mode of delivery or the type of anesthesia used significantly affects the outcome. Respiratory distress is the principal complication. At postmortem examination, pulmonary hyaline membranes and atelectasis have been the only findings in two-thirds of the infants who die. Hypoglycemia, infections, and congenital anomalies play a minor role in the high neonatal mortality rate. The use of antibiotics, oxygen, mist, or cortisone is not helpful in either the prevention or the treatment of hyaline-membrane disease in these infants. Instead, one has to rely on good pediatric care and general supportive measures. No rational mode of treatment for the infant of the diabetic mother is likely to emerge until the maternal and fetal factors which are responsible for the pathogenesis of pulmonary hyaline membranes are better understood.

Acute Ataxia of Childhood: A Summary of 15 Cases. G. M. Lasater and J. T. Jabbour. A. M. A. J. Dis. Child. 97:61-65 (Jan.) 1959 [Chicago].

Acute cerebellar ataxia is usually a benign disorder subsiding in a few days or weeks. It rarely occurs in adults. The etiology is often undetermined, but in most cases it is thought to be a cerebellar encephalitis of infectious or toxic origin. The authors present a summary of the clinical picture and a discussion of possible etiologies based on reports in the literature and their own observations of 15 cases. The ages of the 15 children ranged from 2 to 12 years, all but 2 being less than 8 years old. The most characteristic clinical feature is the abrupt onset of a grossly ataxic gait. This often occurs in a previously well child and sometimes during the convalescent phase of one of the childhood viral infections. The usual story is that the child awoke in the morning or from his afternoon nap and fell upon attempting to walk. It is then discovered that he walks with a staggering gait, falling frequently. Some patients have intention tremors of the upper extremities. Occasionally nystagmus, dysarthria, hypotonia, and dysmetria are also demonstrated. At times there are signs of dysfunction in other parts of the nervous system, such as lethargy, cloudy sensorium, myoclonic movements, and cranial nerve palsies. There is usually no nuchal rigidity. Fever, nausea, and vomiting may be present. The spinal fluid is often normal but may contain a moderate excess of mononuclear cells and protein. Recovery occurs within 1 week to 8 months, usually in 1 to 3 weeks.

Observations on the 15 children suggested mumps, poliomyelitis, influenza, varicella, and intoxication from insecticides as possible etiological agents. Acute ataxia has also been reported in association with rubeola, rubella, smallpox, scarlet fever, typhoid, infectious mononcleosis, diphtheria, and drug intoxication. The prognosis for complete recovery is good.

Occasionally, symptoms caused by a cerebellar tumor may develop acutely, and this lesion must always be considered in children with acute ataxia. Headache and vomiting are more common with cerebellar tumors, but signs that should especially alert the clinician to the probability of this diagnosis are papilledema, tilting of the head, unilateral dysmetria, nystagmus which is more marked in one direction, 6th nerve palsy, high spinal fluid pressure, and x-ray findings of separation of the sutures, erosion of the clinoid processes, and increased convolutional markings.

The Antibiotic Prophylaxis of Bacterial Complications of Measles. S. Karelitz and H. D. Isenberg. J. Pediat. 54:1-10 (Jan.) 1959 [St. Louis].

A total of 251 children with measles were observed, 173 of them at home and 78 at the Queens General Hospital in Jamaica, N. Y. The ages of these children ranged from 1 to 14 years. Of the 78 hospitalized children, 31 had complications, such at tracheobronchitis, pneumonia, and nonbacterial encephalitis. Antibiotic prophylaxis was given to only 2 children before hospitalization; the remaining 76 children had no antibiotic prophylaxis before their admission to the hospital. While at the hospital the antibiotic therapy, consisting of penicillin or erythromycin, was given to a total of 51 patients, 25 of whom had complications and 26 had none. All the hospitalized patients recovered, whether they were subjected to antibiotic therapy or not. Of the 26 patients who were hospitalized without complications and who were subjected to antibiotic treatment, only one developed a secondary infection; this one child who had been given a diagnosis of measles was found to have influenzal meningitis on the 5th hospital day.

Of the 173 children with measles observed at home, the antibiotic therapy was administered to 88, and the antibiotic prophylaxis to 18. Complications occurred 1 to 11 days after the antibiotic treatment had been discontinued in 14 of the 88 patients. These complications included pneumonia in 1 patient, bronchitis in 1, and otitis media in 12. No complication was manifested during the prophylactic treatment. Complications, such as otitis media and pneumonia, occurred in 18 patients who were not subjected to prophylactic treatment.

The higher complication rate observed in the hospitalized children may be attributed to (1) the difference in the social environment of the 2 groups, (2) the younger age of the children, and (3) the complications already manifested by the children at the time of their hospitalization. The authors emphasize the importance of the prophylactic use of antibiotics in very young and weak children with measles in whom the occurrence of complications could be a threat.

Intravascular Red Cell Aggregation in Children with Heart Disease. F. Arajärvi. Ann. paediat. Fenniae. 4:249-255 (no. 4) 1958 (In English) [Helsinki].

A method is available which makes it possible to observe conjunctival blood vessels and the blood cells circulating in them with the aid of a capillary microscope. In healthy adults and children the red blood cells flow along in the smaller vessels in single or double files; in the larger vessels they flow in a homogeneous mass. In many abnormal conditions, though, the red blood cells adhere in clumps; this adherence is visible in the conjunctival blood vessels as a break-up of the files in the smaller vessels and as definite clumps in the larger ones. The author tried to find answers to the following questions: 1. Do vascular disturbances due to congenital heart disease cause aggregation of the red blood cells? 2. Is there any noticeable difference in the appearance of the intravascular aggregation of the red blood cells if the child has a congenital heart disease or rheumatic fever? 3. Is this method of investigation helpful in the cyanotic newborn infant, particularly in the detection of congenital heart disease?

With the aid of a stereomicroscope, conjunctival blood vessels and the blood cells circulating in them were examined in 96 children. In 48 children with congenital heart disease, no red blood cell aggregation was present unless the child had also an infection, but in 23 children with active carditis, red blood cell aggregations could be found. When the conjunctival blood vessels of 20 newborn infants who were cyanotic were examined with the stereomicroscope, red blood cell aggregations could be found in those who had infections (pneumonia, encephalitis) or brain hemorrhage, but no red blood cell aggregations were found in those with congenital heart disease. This proves that this examination is of value in the differential diagnosis of cyanosis in newborn infants.

Intravascular Red Cell Aggregation in Children with Benign and Malignant Tumors. T. Arajärvi and G. R. Wallgren. Ann. paediat. Fenniae. 4:256-263 (no. 4) 1958 (In English) [Helsinki].

The studies described in this paper were carried out to ascertain: (1) whether a tumor can cause red blood cell aggregation; (2) whether there is any difference in this respect between a benign or a malignant tumor; and (3) whether the aggregation test might be an aid in the early diagnosis of cancer. The stereomicroscope was used in the study of the red blood cells circulating in the conjunctival blood vessels of 100 children who had been hospitalized because of a proved or suspected tumor. The diagnosis was confirmed in all the children by histopathological examination. Red blood cell aggregation was very mild or completely absent in the children with benign tumors or with congenital anomalies. In the children with malignant tumors the red blood cell aggregation was definite. However, aggregation of red blood cells was present also in children who had an infection in addition to a benign tumor or who had only an infectious disease instead of the suspected tumor. The degree of the red blood cell aggregation was proportional to the increase in the sedimentation rate and to the decrease in the hemoglobin value in the children with malignant tumors.

DERMATOLOGY

Chronic Penicillin Urticaria from Dairy Products, Proved by Penicillinase Cures. M. C. Zimmerman. A. M. A. Arch. Dermat. 79:1-6 (Jan.) 1959 [Chicago].

Penicillin is widely used to treat mastitis in cattle. From this use it contaminates, according to an estimate made in 1957, 11% of American milk samples. The contamination of dairy products by traces of penicillin has previously been suspected but never proved as a cause of allergic reactions. The author reports on 3 men and 1 woman in whom proof of the allergenicity of penicillin in dairy products has been based on the following evidence: 1. All the patients had previous allergic reactions (urticaria) to penicillin. 2. The previously known allergic reaction to penicillin was duplicated repeatedly after ingestion of dairy products. 3. The reaction cleared rapidly after injection of 800,000 units of penicillinase (Neutrapen), a penicillin-destroying enzyme with no effect on anything but penicillin. 4. The patients were able to eat dairy products without subsequent allergic reaction if given a prophylactic injection of penicillinase first.

Patients with chronic urticaria in whom penicillin sensitivity is suspected should be given a test injection of penicillinase. If urticaria clears for 4 to 7 days, penicillin sensitivity has probably been the cause. Patients with chronic urticaria, in whom penicillin sensitivity is proved or suspected, should have such dairy products as milk, ice cream, and Roquefort or bleu cheeses containing Penicillium species molds eliminated from their diets. If patients have a flare-up 4 to 7 days after a penicillinase injection, there is residual penicillin in the system which has not been destroyed. Penicillinase injections should be repeated at 4-to-7-day intervals, as necessary, to stop symptoms. If more than 8 days pass before a new outbreak of allergic symptoms after an injection of penicillinase, then the penicillinase has destroyed all the penicillin in the system at that time. A new outbreak suggests either that the patient has had a new exposure to penicillin or that his new reaction is due to some other allergen.

Smooth-Muscle Tumors of the Skin. H. Montgomery and R. K. Winkelmann. A. M. A. Arch. Dermat. 79:32-41 (Jan.) 1959 [Chicago].

The authors report on 33 patients with smooth-muscle tumors of the skin on whom biopsies were performed at the Mayo Clinic. Of the 33 patients, 23 had leiomyoma cutis, 8 had angiomyoma, 1 had nodular or so-called dartoic myoma, and 1 had leiomyosarcoma. The ages of the 8 male and 15 female patients with leiomyomas ranged from 10 to 20 years at the time of onset of the clinical signs. The lesions were located on the face, trunk, or extremities; they progressed slowly and became painful when they were large enough to invade and extend around the bundles or trunks of cutaneous nerves in the deeper part of the cutis and the subcutaneous tissue. Special stains did not reveal any increase in nerve fibrils or nerve trunks. Special histochemical stains proved to be of little value in identifying myomatous tissue. All the angiomyomas occurred as solitary lesions, and all the 8 patients were women. The age of onset was much later in this group than in that with leiomyomas, which sometimes began at birth or shortly thereafter. Dartoic myoma, which occurred in the scrotum of a 54-year-old man, is an uncommon lesion seen primarily by the surgeon because it begins in the subcutaneous tissue and calls for surgical removal. A painful leiomyosarcoma of one year's duration was removed surgically from the right thigh of a 32-year-old woman; the patient apparently had no recurrent tumors 21 years after the surgical excision. Smooth-muscle tumors may be allowed to remain in situ as long as they are asymptomatic. When treatment is desirable, surgical excision is the method of choice. Radiotherapy apparently has no effect on the lesions or the sensations that they produce.

Granuloma Faciale. W. C. Johnson, R. S. Higdon and E. B. Helwig. A. M. A. Arch. Dermat. 79:42-52 (Jan.) 1959 [Chicago].

The authors report on 14 men and 1 woman with granuloma faciale, a dermatosis characterized clinically by elevated, usually asymptomatic, reddish-brown plaques on the face. Tissue sections from the lesions of these patients were examined at the Armed Forces Institute of Pathology for the purpose of determining the natural history of granuloma faciale and its relation to eosinophilic granuloma and of exploring its histogenesis. In 12 of the 15 patients the clinical aspect of the disease was that of a plaque or nodule, and in the remaining 3 it was that of a macula. The lesions were soft, usually brown, red, or purple, and varied from a few millimeters to 8 cm. in diameter. New lesions developed over a period of several months in some of the patients. Five patients were asymptomatic, but 10 noticed varying degrees of itching, burning, stinging, or tenderness. Response to therapy other than wide excision was poor. The lesion in most patients tended to persist indefinitely but varied in color and substance from time to time. The general health of the patients remained good.

No evidence was found of any relationship between granuloma faciale and eosinophilic granuloma of bone or the heterogeneous conditions once called eosinophilic granuloma. The authors' observations suggest that the pathogenesis of granuloma faciale is basically an antigen-antibody or hypersensitivity reaction, the small blood vessels and perivascular tissues in the upper corium of the face being the "shock" tissues. The exciting factors remain unknown, but foci of infection, photosensitivity, trauma, and drugs must be considered.

Genetic Studies on Acanthosis Nigricans. H. O. Curth and B. M. Aschner. A. M. A. Arch. Dermat. 79:55-66 (Jan.) 1959 [Chicago].

The authors carried out genetic studies on patients with acanthosis nigricans at the department of dermatology of the College of Physicians and Surgeons of Columbia University in New York. Three types of this dermatosis have been recognized, namely, benign acanthosis nigricans, malignant acanthosis nigricans, and pseudoacanthosis nigricans. Family studies of 13 patients with the benign type of the disease revealed 9 families in which more than one member was affected. Altogether, there were 27 instances of benign acanthosis nigricans in these 9 families, 14 of the patients being males and 13 females. These figures suggest a genetic background for the benign type of acanthosis nigricans, which shows either regular or irregular dominance. Pseudoacanthosis nigricans, secondary to excessive obesity, may be considered a phenocopy of benign acanthosis nigricans. Pseudoacanthosis nigricans was not included in the authors' genetic studies because environmental factors, such as food intake and personal hygiene, seem to have played a significant role in the pathogenesis of the disorder.

No familial case of malignant acanthosis nigricans has been found. Family studies of 26 patients with the malignant type of the disorder revealed one consanguineous marriage among the parents of the 26 patients. The series of families studied is too small to permit this incidence to be considered as an indication of recessive inheritance of malignant acanthosis nigricans. Family members of patients with malignant acanthosis nigricans were examined also for cancer without acanthosis nigricans. No specific trend with regard to frequency and location of tumors in the relatives of the 26 probands was seen, and cancer did not occur in the relatives of 14 (54%) of these probands. In 24 of the 26 probands with malignant acanthosis nigricans, the two parents in each case had an identical ethnic background. The possibility of a genetic basis for the whole syndrome of malignant acanthosis nigricans, as for part of it, has been discussed. The tumors associated with maligant acanthosis nigricans, although originating in various organs, show similar clinical behavior and similar morphology in that they all are adenocarcinomas; the specificity of these tumors, however, has not as yet been established. The percentage of gastric cancers among the cancers associated with malignant acanthosis nigricans has been high. The fact that no instance of transition from the benign to the malignant form or of occurrence of both types in one family has ever occurred confirms the assumption that benign and malignant acanthosis nigricans are separate diseases.

Fungistasis of Hydrocortisone and Certain of Its Analogues. R. L. Sauvan and R. L. Sutton Jr. A. M. A. Arch. Dermat. 79:53-54 (Jan.) 1959 [Chicago].

The authors tested the fungistatic properties in vitro of hydrocortisone acetate and hydrocortisone alcohol in 0.1 and 0.9% concentrations and of prednisolone phosphate and prednisolone alcohol in 1.0% concentrations. The organisms selected for testing were common dermatophytes: Trichophyton rubrum, T. gypseum, Microsporum audouini, M. canis, and Candida albicans. Results of the tests showed that the hydrocortisones and the prednisolones in the concentrations used did not display fungistatic properties against the fungi tested. C. albicans grew well under conditions adverse to the growth of T. gypseum, M. audouini, T. rubrum, and M. canis.

OTOLARYNGOLOGY

The Auditory Manifestations of Leukemia. E. Shanbrom and S. C. Finch. Yale J. Biol. & Med. 31:144-156 (Dec.) 1958 [New Haven, Conn.].

The records of the last 100 patients with leukemia admitted to the Yale-New Haven Medical Center were reviewed for evidence of acoustic difficulties. All patients with leukemia, irrespective of age, sex, and type of leukemia, were included. Thirty-two of the patients in this group had definite auditory signs or symptoms. In 16 there was a well-established relationship between the leukemia and the development of these disorders. In an additional 11 there was an almost certain but less definite relationship. There were 6 instances in which an otological complication presented as the only symptom or as part of the initial complaints which brought the patient to the hospital. Four of the 6 patients had acute leukemia. In the others the auditory difficulties developed in the course of the leukemia. In 5 of the 32 patients it was clear that the leukemia was not responsible for the auditory disorders. The most frequent auditory symptoms in the 27 patients were deafness in 16, tinnitus in 7, and pain in 3; only 1 patient complained of vertigo. A few patients were asymptomatic but had bleeding or purulent drainage from an external canal. The term "deafness" is employed to imply varying degrees of hearing loss.

The incidence of otological complications due to leukemia in this small series is 27%. Without the aid of histological examination it was difficult to be sure of the pathophysiology of some of the instances in which acoustic difficulties were encountered. In general, however, patients in whom hemorrhage was responsible usually had acute leukemia. Obstruction of the eustachian canals due to lymphoid hyperplasia was encountered only in chronic lymphocytic leukemia. Infection of the middle ear showed no predisposition to any particular type of leukemia. Auditory difficulties were commoner and developed earlier in patients with acute leukemia than in those with chronic leukemia.

Relief of Deafness by Stapes Mobilization. E. H. M. Foxen. Brit. M. J. 2:1558-1561 (Dec. 27) 1958 [London].

The author traces the history of stapes mobilization from 1875 when probably Kessel carried out the first mobilization. After a dormant period of half a century the operation was resurrected by Rosen in 1952. Stapes mobilization is most commonly indicated in cases of otosclerosis in which fenestration would have been advised formerly, and it is noteworthy that stapes mobilization is more general in its application than fenestration of the labyrinth. The diagnosis of otosclerosis should be firm and the hearing loss reasonably symmetrical. Pure-tone audiometry should ideally show a 35-to-55-db. loss of air conduction for the critical speech frequencies with a satisfactory air-borne gape (preferably at least 20 db.). Amplification should be well tolerated, paracusia present, and Schwartze's sign absent. Local analgesia is preferred but is not obligatory. After the incudostapedial joint and the surrounding anatomic structures have been displayed, maneuvers aimed at freeing the stapes are carried out. If mobilization is found to be impossible, fenestration of the stapes footplate is undertaken. The progress of the operation is controlled by hearing tests at intervals. Absorbable gelatin sponge (Gelfoam) provides a suitable dressing and may be retained by a strip of ribbon-gauze, which is removed after 2 to 4 days. As a rule, no particular sedation is required, and the patient is usually discharged on the 4th or the 5th postoperative day. Penicillin is given regularly during this time.

A comparison between features of stapes mobilization and fenestration shows that, when such matters as length of stay in the hospital and postoperative discomfort are considered, the magnitude of the former operation is much less than that of the latter. Results to date suggest that, of the patients undergoing stapes mobilization, about 33% may be expected to obtain a useful, lasting, and, in some cases, great hearing improvement; 33%, a slight improvement; and the remainder, no improvement. In a patient in whom the result is disappointing, the fact that the operation may have been performed several times does not preclude him from undergoing fenestration of the labyrinth at a later date.

THERAPEUTICS

Reversal of Intractable Cardiac Edema with Prednisone (Meticorten). D. A. Newman. J. Florida M. A. 45:778-782 (Jan.) 1959 [Jacksonville].

Ten patients with intractable cardiac edema were subjected to treatment with steroid preparations, principally prednisone. There were 7 men and 3 women, ranging in age from 60 to 85 years. All had arteriosclerotic heart disease, which was associated in 6 with hypertension; 5 of the patients had had myocardial infarction previously. Two patients had aortic regurgitation; 1 had pericardial calcification and constriction; 1 had diabetic glomerulosclerosis with the nephrotic syndrome; 3 had associated bronchopulmonary disease; and 1 had a recognized but quiescent duodenal ulcer. All these patients had been under treatment for congestive heart failure for 2 or more years. Since the standard therapeutic measures had been exhausted, they had become unresponsive to mercurials, to chlorothiazide, to aminophylline, and to such other treatments as induced hyperchloremic acidosis by the combined use of ammonium chloride and Diamox. These patients were considered as calculated risks and were treated accordingly with appropriate countermeasures.

Treatment with corticotropin (ACTH) was attempted in the first of the 10 patients in the series, but it proved a failure. A second patient who was treated with prednisone died after a cerebrovascular accident, but a good remission was obtained with this drug in the remaining 8 patients. The administration of prednisone was started in daily doses of 2.5 mg. This dosage was cautiously increased to between 15 and 20 mg. a day for 4 or 5 days and was then gradually decreased over a varying time interval, depending on each patient's response to the mercurial given after the priming with prednisone. With the onset of diuresis the daily maintenance dose varied from 2.5 to 10 mg. No other change in standard therapy for congestive heart failure was instituted. The intake of water and fluids was neither restricted nor enforced, except in 2 patients with hyponatremia; in the case of these patients a moderate restriction of fluids to 1 or 1.5 liters a day was recommended. Salt restriction was urged to a maximum of 1 Gm. per day. Ammonium chloride was given for one day before, one day during, and one day after the mercurials, when these were given by injection.

The most gratifying feature in the 8 patients who obtained remission with prednisone was the subsequent return of responsiveness to diuretics—not only to injection of mercurials in much smaller doses than previously but also to Diamox, to chlorothiazide, and even to the oral administration of Neohydrin. Diamox seemed to be unusually effective in the patients with additional bronchopulmonary disease and in the one with constrictive pericarditis. Five of the 8 patients have remained in good compensation for periods ranging from 9 to 28 months, but the other 3 have died. The first of these, a 76-year-old man with pericardial constriction and previous myocardial infarction, who had been in excellent compensation for more than 2 years on 2 tablets of Diamox a week and 2.5 to 5 mg. of prednisone a day, died suddenly of pulmonary embolism after he had discontinued this medication in favor of chlorothiazide without prednisone. The second patient died at the age of 74 years of an acute myocardial infarction 9 months after the initially successful reversal of the intractable cardiac failure. The third patient died at the age of 69 years of bronchopneumonia 14 months after a similar successful reversal. The intervening period of maintenance treatment had been most satisfactory as regards both relative comfort to the patient and general ease of management.

Clinical Evaluation of Povidone-Iodine Aerosol Spray in Surgical Practice. A. L. Garnes, E. Davidson, L. E. Taylor and others. Am. J. Surg. 97:49-53 (Jan.) 1959 [New York].

The authors used the complex of iodine and polyvinylpyrrolidone (povidone-iodine) in the form of an aerosol spray (Betadine Aerosol Spray) as an antiseptic and germicide in the preparation of 200 patients with lacerations for emergency suture, in the preparation of the skin in major surgical interventions on 100 patients, in the treatment of 16 patients with severe burns, and in the treatment of 15 patients with stasis ulcers of the leg. The wounds of all the patients with lacerations healed per primam without side-reactions or evidence of local irritation. Bacteriological cultures taken from the sites before and after operation indicated that all pathogenic agents were eliminated by wiping the skin dry and spraying the Betadine aerosol over an adequate surface; the only remaining organisms were saprophytes and diphtheroids. Biopsy of a skin specimen showed no penetration of the epidermal layers. Although most of the 100 patients subjected to major surgical procedures had established peritonitis or peritonitis due to spillage of intestinal contents, there were no wound infections in this group of patients and all operative incisions healed per primam.

In the patients with second-degree and third-degree burns, treated by spraying with the Betadine aerosol every 12 hours for the first 72 hours and daily thereafter until separation of the eschar began, the medication and method of application facilitated the open therapy of burns, providing a protective covering for areas denuded of skin. The antiseptic properties of the spray controlled infection and inhibited odor. Severely burned children found this form of treatment acceptable. In the patients with stasis ulcers, the lesions were sprayed twice or three times weekly with the Betadine aerosol, and compression bandages were applied. No side-reactions or satellite ulcers developed. The antiseptic agent aided in the maintenance of an environment ideally suited for healing. Even when it was applied to large, open wounds, discomfort was mild and transitory. Protein-bound iodine determinations did not reveal appreciable change in pretreatment and post-treatment levels. Providone-iodine spray is a safe, time-saving, effective antiseptic and germicide for surgical wounds, burns, and *stasis* ulcers.

Palliative Chemotherapy of Solid Tumors with Nitromin. R. G. Mrazek and S. G. Economou. A. M. A. Arch. Surg. *78*:51-55 (*Jan.*) 1959 [Chicago].

The authors report on 48 patients with various advanced malignant tumors who were treated with Nitromin at the tumor clinic of the Research and Educational Hospitals of the University of Illinois in Chicago. An average dose of 402 mg. was given, usually as 50 mg. per day. The drug was administered by the intravenous, intraperitoneal, or intrapleural route. Nitromin is an alkylating agent which was developed during the search for compounds which would have the therapeutic effect of nitrogen mustard with lessened toxicity. Of the 48 patients, 4 had malignant lymphoma, 5 had adenocarcinoma of the stomach, 8 had adenocarcinoma of the colon and rectum, 2 had adenocarcinoma of the pancreas, 4 had tumors of the kidney, 10 had bronchogenic carcinoma, 5 had squamous-cell carcinoma, 4 had malignant melanoma, 1 had carcinoma of the breast, and 5 had miscellaneous tumors. Two of the 4 patients with lymphoma showed reduction in fever and diminution in the size of the spleen and liver. Formation of pleural fluid was reduced in one patient with bronchogenic carcinoma and in one with metastatic adenocarcinoma of the thyroid gland. One patient with adenocarcinoma of the stomach with liver metastases had an improved sense of well-being, an increase in appetite, and relief of pain. These 5 patients obtained relief with relatively small total doses of Nitromin, 200 to 500 mg., whereas as much as 800 mg. was given to the other 43 patients with no effect; 24 of the latter are dead. Side-effects, such as nausea and vomiting, were frequently seen, but severe leukocyte depression was observed only in 3 patients. Nitromin did not cause local irritation or venous thrombosis.

The almost uniformly discouraging results in these patients with far-advanced carcinoma contrast completely with the well-documented demonstration that Nitromin can completely free rats of Yoshida ascites sarcoma implants, if given when the tumors are still small. The authors agree with Ishidate and Druckrey that Nitromin might be effective in patients with tumors in the early stages, or when administered in combination with surgical treatment to destroy microscopic tumor remainders, or when given intravenously after operation to destroy free cells in the blood. Nitromin has the advantages of low toxicity, ease of injection, and relative freedom from side-effects.

Chlorothiazide (Chlotride) in Edema: Clinical Tests with a Mercurial Diuretic. D. Jensen and H. S. Mathisen. Tidsskr. norske lægefor 78:1166-1170 (Dec. 1) 1958 (In Norwegian) [Oslo].

Twenty-eight patients (average age, 68½ years) were treated with chlorothiazide for from 3 to 9 days because of edema. In all, 61 treatments were given. The chlorothiazide dose was usually 0.50 Gm. daily, i. e., ½ tablet twice daily, preferably in the morning and at noon; in 5 tests 1 Gm. was given daily, in 2 cases the dose was reduced to 0.25 Gm. daily. The average increase in diuresis was about 70% daily; the average loss of weight during the time of treatment was 0.31 kg. (¾ lb.) daily. The maximal increase in diuresis averaged 143%, with variations between 29 and 323% in the different periods of treatment. The authors found that chlorothiazide seems to approach the ideal diuretic. It was in several tests equal to or superior to mersalyl and better than other diuretics tried for oral use. With the dosage applied, the agent was practically free from side-effects.

Pathological and Biochemical Considerations on Chronic Alcoholism with Relationship to the Therapeutic Effect of Liver Extracts Administered Intravenously. P. Benassi and D. Munarini. Minerva med. 49:4334-4341 (Nov. 24) 1958 (In Italian) [Turin, Italy].

Intravenous administration of Ripason, an Italian proprietary liver-extract preparation, had a beneficial effect on 30 chronic alcoholic patients. Before the treatment the tolerance of each patient was tested by parenteral administration of 1 cc. of this liver extract; during treatment the patient received a daily dose of 3 or 4 cc. The preparation was always introduced into the vein with some rapidity. Twenty patients were treated for 30 days and 10 patients for 60. The drug was well tolerated and did not cause undesirable side-effects during or after its injection. Clinically, an improvement, at times very marked, of the general condition and of the metabolism followed in all the patients; the appetite increased and the cenesthesia improved markedly. Psychologically, the preparation had a beneficial antidepressive effect on the adjustment of the patients to the environment, and caused improvement in their daily work and general behavior. The group of patients who received treatment for 2 consecutive months showed improvement in the Takata, Wuhrman-Wunderly, and Kunkel laboratory tests.

A New Treatment for Cutaneous Larva Migrans: Employing Oral Promethazine. J. L. Greene. J. Florida M. A. 45:784-788 (Jan.) 1959 [Jacksonville].

The oral administration of promethazine (Phenergan) hydrochloride to 57 patients with creeping eruption caused by larva migrans is reported. The group included both sexes and ranged in age from 14 months to 68 years. The patients presented skin lesions on various parts of the body, but the extremities, the back, and the perineum were more frequently involved. The compound was administered at bedtime—as a sirup to children up to the age of 6 years in doses of 50 mg. and as tablets to older children in doses of from 75 to 100 mg.; adults were given oral doses of 150 mg. or more. The same doses were given on 3 successive nights, and occasionally it was necessary to repeat the course with the same amount or with an increased dosage.

The oral administration of promethazine was a failure in the first 6 patients (10.5%) who were given only small doses (25 mg.) of the drug. The pruritus, however, promptly disappeared in all the remaining patients (89.5%) after the first larger doses of promethazine were given; at the same time the marked redness and the prominence of the skin lesions began to fade, and healing was complete within 3 or 4 days. The soporific properties of promethazine, which are entirely separate from the activity of the compound upon the larva, were an advantage to these patients, since insomnia caused by intense itching is one of the consequences of cutaneous larval infestation. The hyperexcitability exhibited by some patients after the ingestion of the first dose of this compound may be promptly controlled by an additional dose, and this reaction does not represent a contraindication to the use of the compound. The success obtained solely by the oral administration of promethazine is of great interest, since all treatments so far suggested for cutaneous larva migrans have been disappointing.

Absorption of Orally Administered Vitamin B_{12} in Pernicious Anaemia. J. N. M. Chalmers and N. K. Shinton. Lancet 2:1298-1302 (Dec. 20) 1958 [London].

Fifteen men and 6 women, between the ages of 43 and 82 years, with pernicious anemia in relapse were treated for 15 days with daily doses of vitamin B_{12} given orally alone. The amount of vitamin B_{12} given ranged from 20 to 500 mcg. daily. The larger the daily dose of vitamin B_{12} given orally, the more prompt was the hematological response and the return of the serum vitamin B_{12} level to the normal range. Long-term maintenance therapy with daily doses of vitamin B_{12} was given orally to 12 patients, 3 of whom received doses of 50 mcg. daily for periods ranging from 21 to 50 months, 3 received doses of 100 mcg., 2 received doses of 200 mcg., and 4 received doses of 500 mcg. daily for periods ranging from 6 to 26 months. Results showed that daily doses of 100 mcg. or more of vitamin B_{12} given orally can be effective in maintenance therapy. These findings provide further proof that vitamin B_{12} given orally can be absorbed and utilized by patients with pernicious anemia. Some of the patients obtained normal hematological values and clinical remissions without return of serum vitamin B_{12} level to normal. Parenteral therapy with vitamin B_{12} is still the most reliable method of ensuring freedom from relapse in pernicious anemia, but with the close cooperation of the patient oral treatment by daily application may be effective.

Vitamin B_{12} in Pernicious Anemia: Intramuscular or Oral? E. H. Hemsted and J. Mills. Lancet 2:1302-1303 (Dec. 20) 1958 [London].

The authors compared the effects of oral and intramuscular administration of vitamin B_{12} in patients with pernicious anemia treated at the Royal Berkshire Hospital in Reading, England. Over a period of 2 years a group of 71 patients taking a daily dose of 100 mcg. by mouth one hour before breakfast were maintained at least as well as a group of 84 patients receiving a monthly intramuscular injection of 100 mcg. Thirty-four patients with pernicious anemia were treated for 2 years with intramuscular injections of 1,000 mcg. of vitamin B_{12} per month; there was no significant change in hemoglobin and red blood cell levels, and, therefore, no advantage in a higher dose than 100 mcg. per month for maintenance treatment was apparent.

PATHOLOGY

Coccidioidal Pulmonary Cavitation. L. Hyde. Am. J. Med. 25:890-897 (Dec.) 1958 [New York].

The author reports on 76 men and 1 woman with coccidioidal pulmonary cavitation, 57 of whom were studied at the Veterans Administration Hospital in Long Beach, Calif., and 20 were included in the Veterans Administration–Armed Forces Cooperative Study of Coccidioidomycosis. The median age was 25 years; 90% were under 40 years of age. Coccidioidal pulmonary cavitation occurred in 2 or 3% of those patients in whom primary infection due to Coccidioides immitis was severe enough to cause consultation of a physician. Fifty-eight per cent of the whole group were essentially asymptomatic, and the condition was detected on the taking of routine chest roentgenograms; 26% were subjected to roentgenography because of hemoptysis, 6% because of chest pain, and 10% because of acute respiratory symptoms. In most of the patients who gave a history of bleeding, there had been only minimal blood streaking or a small hemoptysis. Cavitation in this disease occurs at the site of the original coccidioidal pneumonia. Generally there are no signs or symptoms during the process of cavitation in hospitalized patients. Eighty-six per cent of the 77 patients in this series had a single cavity, and 14% had multiple cavities. Fifty-eight per cent of the cavities were in the right lung, and 42% in the left lung; 3 patients had bilateral cavities. The results of the coccidioidin skin test were positive in 57% of the 73 patients for whom the results were recorded. In most cases the skin test was made once, but for some it was repeated on numerous occasions. Sixty-four per cent of the 77 patients had positive complement-fixation antibodies in varying degrees.

Nonsurgical and surgical treatment in patients with coccidioidal pulmonary cavitation has been compared. Forty-six per cent of the whole group were treated nonsurgically. Most patients were asymptomatic, but 22% of this group had a history of bleeding; no new cavities developed in any of the 36 patients. Fifty-four per cent of the 77 patients underwent resectional surgery. Twenty-nine of these patients were asymptomatic, although 30% gave a history of bleeding. There were no deaths, but in 29% of the patients who had resection, bronchopleural fistulas with empyema developed, and 20 additional surgical procedures were required. Furthermore, new cavities appeared postoperatively in 20% of the patients who underwent resection. On the basis of these findings a conservative nonsurgical treatment appears most desirable for patients with coccidioidal pulmonary cavitation, unless the cavity is more than 4 cm. in diameter or is enlarging significantly or there have been recurrences of severe hemoptysis.

Incidence and Prognosis in Cancer of the Rectum in a Danish Provincial Town. N. Blixenkrone-Møller. Danish M. Bull. 5:268-272 (Dec.) 1958 (In English) [Copenhagen].

From 1946 to 1955, 180 cases of rectal cancer, in 112 men and 68 women, were diagnosed in Aarhus (population of about 113,000). In all but 10 cases the diagnosis was confirmed by histological examination; in 6 of the 10 there were metastases, and 4 were clinically unquestionable. Most cases occurred between the ages of 60 and 70 years. Up to the age of 60, cancer of the rectum is equally frequent in men and women; a steep rise then occurs among men. The lower margin of all tumors was at a level of 20 cm. or less from the anus at proctoscopic examination. Of the 170 cases examined histologically, 158 were adenocarcinomas; 6, solid carcinomas; 5, malignant papillomas, with typical invasive growth; and 1, a lymphosarcoma. Diagnosis was made within the first 3 months after the onset of the first symptom in only 42% of the cases. About 30% of the cases were radically inoperable. Major radical operation was performed on 98 of the patients with radically operable cancer. Of these, 37% were living 5 years later, or, corrected for deaths from unrelated causes, 43%. Of the entire group of 180 patients, only 20% were living after 5 years. A few had died of causes other than cancer. The prognosis is better for the age group under 60. There was no demonstrable difference in the prognosis for men and for women. The analysis shows that removal of skin and pelvic connective tissue must be more radical.

Fat Embolism in Chronic Alcoholism: Control Study on Incidence of Fat Embolism. M. J. G. Lynch, S. S. Raphael and T. P. Dixon. A. M. A. Arch. Path. 67:68-80 (Jan.) 1959 [Chicago].

The changes found in the central nervous system in association with chronic alcoholism appear to be ill-defined. Wernicke's "superior hemorrhagic polioencephalitis" was specifically linked to chronic alcoholism, and Gudden's atrophy of the corpora mammillaria was somewhat later similarly associated; however, subsequent observations cast much doubt on the specificity of the association between the Wernicke-Gudden changes and alcohol addiction. It is now accepted that the lesions described by these pioneers are due to concomitant vitamin deficiencies. Although general dietary improvement has altered the neuropathological picture of chronic alcoholism, certain diffuse or patchy, ill-defined, and apparently nonspecific changes, such as loss of neurons, focal degenerative lesions, atrophy, and astrocytic proliferation, remain to be explained.

The interest of the present authors in this problem was aroused by the work of Hartroft and Ridout, who demonstrated that in rats fed on choline-deficient diets "fat cysts" develop in the livers and that such large fat globules may rupture into biliary or vascular channels. These workers examined human autopsy material from 30 cases of chronic alcoholism and found "small amounts of embolic fat within the vessels of the lungs and kidneys in a number of cases." In preliminary studies on 250 consecutive autopsies, the present authors found fat embolism only in cases of trauma, alcoholic fatty liver, and necrotizing pancreatitis. However, in that series only one block each from lung and kidney was examined, and these were not uniformly selected as to size or site. For the present investigation a more thorough study was planned, and a block from each lung was selected and examined.

From the beginning of 1957 to the present time the authors have made studies on 51 patients with alcoholic psychosis admitted to their psychiatric unit. Morning sputum samples were examined for fat droplets, which were found in 48 of them. The 3 patients with sputums which were negative for fat globules had little more than "hangovers." The authors conclude that fat embolism is of common occurrence in chronic alcoholics. Fat embolism is advanced as a major factor in the etiology of alcoholic psychoses and may lead to death in some such cases. Repeated fat embolism may be the basis of some, at least, of the changes noted in the brains of chronic alcoholics.

Rheumatic Pneumonitis: Pathological Features. R. F. Scott, W. A. Thomas and J. M. Kissane. J. Pediat. 54:60-67 (Jan.) 1959 [St. Louis].

Autopsy was performed on 87 children, ranging in age from 3 to 16 years, who died of pneumonitis due to rheumatic fever during 1919-1954 at the St. Louis Children's Hospital. Microsections of the lungs were examined especially for fibrinous exudate in the alveolar sacs or respiratory ducts, hyaline-like membrane, and necrosis of the alveolar walls and thrombi. Pathological changes were graded as "slight" if less than 10% of the tissue available for miscroscopic study was estimated to be involved, "moderate" if 10 to 20%, and "advanced" if more than 20%. With this criterion, 21 cases (39%) showed slight pathological change; 29 (54%), moderate change; and 4 (7%), advanced change. The cases were divided into 3 age groups—3 to 5 years, 6 to 10 years, and 11 to 16 years. The incidence of rheumatic pneumonitis in each group was as follows: 8 of 11 cases (73%) in the youngest group; 24 of 32 cases (75%) in the intermediate group; and 24 of 44 cases (55%) in the eldest group. Gross findings were not distinctive. Most anatomic specimens revealed only congestion and edema; only occasionally were there grayish-red and firm lungs which exuded little fluid and were suggestive of rheumatic pneumonitis. Histologically, the most characteristic feature was a patchy, dense, fibrinous exudate in the alveolar sacs and in the respiratory ducts. This exudate was in the form of irregular globular masses or membranes and was almost invariably associated with monocytes (many containing hemosiderin) and protein-rich edema fluid. Intra-alveolar hemorrhage was common. No consistent difference was found between the anatomic features -seen in pneumonitis due to rheumatic fever and those in pneumonia associated with other diseases.

Histomorphologic Study of the Changes of Arterial Walls from Birth Until the Age of Twenty, with Particular Reference to the Coronary Arteries. M. Bisiani. Minerva cardioangiol. 6:519-536 (Oct.) 1958 (In Italian) [Turin, Italy].

Histological examination of the walls of the sylvian arteries, of the aorta, of the anterior descending coronary artery, and of a section of renal arteries was made in 56 patients. There were 33 males and 23 females, aged between birth and 20 years. These patients had died of an acute disease, such as acute enterocolitis or acute appendicitis, and none of them had a posthumously observed lesion of a more remote disease. Histological changes and the rate of thickening with age of the aorta and of the sylvian and renal arteries in these patients were gradual and similar, whereas those of the coronary arteries were dissimilar to the changes observed by other workers. The structure of the intima of the coronary arteries started to change after a few weeks of life, while the tunica media and the adventitia appeared normal. At the age of 3 or 4 months a sectional thickening of the subendothelial connective tissue of the coronary arteries was observed in both sexes. Various processes took place in the intima, involving edematous imbibition of the subendothelial mesenchyma, neoformation of elastic fibers, thickening and splitting of internal elastic membranes, and formation of fibroblastic cells, histiocytes, and lymphoids. Endothelial cells also seemed to participate in these precocious changes, exhibiting mild regressive processes. The intima thickened, and gradually larger sections of it became affected with age. After the first decade of life, thickening of the subendothelial mesenchyma involved the whole intima, which was in some sections thicker than the tunica media. The hyperplastic process apparently did not affect the tunica media and only slightly the adventitia. Lipids started to appear when thickening of the intima reached or surpassed that of the tunica media.

Pseudomonas Septicemia: Observations on Twenty-three Cases. C. E. Forkner Jr., E. Frei, J. H. Edgcomb and J. P. Utz. Am. J. Med. 25:877-889 (Dec.) 1958 [New York].

The authors report on 23 patients with malignant neoplastic disease (13 of these patients had acute leukemia, 1 had acute disseminated histoplasmosis, and 1 had mycosis fungoides). In addition, these patients, who were seen at the clinical center of the National Institutes of Health in Bethesda, Md., between 1954 and 1957, had the complication of septicemia due to Pseudomonas organisms. The common clinical manifestations of Pseudomonas septicemia include characteristic cutaneous lesions, progressive jaundice, neurological abnormalities, arrhythmia, ileus, and sudden development of hypotension. Twenty-two of the 23 cases were fatal. The median duration of life after identification of the first positive blood culture was 4 days. The most striking gross and morphologic changes were the cutaneous lesions, which were classified according to the following 4 categories: (1) ecthyma gangrenosum, which mostly occurred in the anogenital area; (2) vesicular lesions, which tended to occur in clusters; (3) flat and sharply demarcated cellulitis, which after rapid enlargement became hemorrhagic and necrotic; and (4) small, pink, round maculopapular plaques or nodules, characteristically found on the trunk. In the course of Pseudomonas septicemia metastatic abscesses may appear in any part of the body. The affinity of Pseudomonas organisms for the walls of small vessels is stressed.

Of the 23 patients in this series, the 13 with acute leukemia were selected, as a group, for the analysis of epidemiology and host resistance. Pseudomonas aeruginosa was the second most frequent cause of septicemia and the most frequent bacterial cause of death on the acute leukemia service. The cases of Pseudomonas septicemia on the acute leukemia service were noted to occur in groups, in contrast to the random distribution of other bacterial septicemias occurring on that service. Gram-negative septicemias occurred more frequently than septicemias due to gram-positive bacteria in patients receiving adrenal steroid therapy. Of the 13 incidences of Pseudomonas septicemia, 10 occurred in patients receiving broad-spectrum antimicrobial therapy, whereas the respective figure for other gram-negative septicemias was only 12 of 22 incidences, and for gram-positive infections only 13 of 39 incidences. These data add to the evidence that Ps. aeruginosa is a common super-infecting organism. There is suggestive evidence that antimetabolite administration may in some way predispose to the development of Pseudomonas septicemia.

Familial True Hermaphrodism in Pre- and Postpuberal Genetic Females: Hormonal and Morphologic Studies. G. W. Clayton, J. D. Smith and H. S. Rosenberg. J. Clin. Endocrinol. 18:1349-1358 (Dec.) 1958 [Springfield, Ill.].

Two siblings with scrotal testes and ovaries are presented. The first, aged 16 years, except for a congenital abnormality of the penis described as "complete hypospadias without cryptorchidism," which had been successfully repaired at age 4, appeared to be a psychologically well-orientated male. Concomitant with the normal puberal changes —growth spurt, increase in size of the penis, appearance of sexual hair, and deepening of the voice, there had been progressive enlargement of the breasts. In retrospect the testes were noted to have remained small and insensitive. The family history was significant in that a 7-year-old brother had a similar congenital abnormality of the external genitalia. A 12-year-old brother was normal. A smear of the buccal mucosa in the 16-year-old sibling demonstrated a positive nuclear chromatic pattern, but urethrograms failed to reveal vestiges of the Müllerian system. Hormonal studies showed a low urinary excretion of 17-ketosteroids, an elevated excretion of estrogens and pregnanediol, and a normal excretion of gonadotropins. The initial impression was Klinefelter's syndrome; however, the familial hypospadias suggested that a more complex type of gonadal dysgenesis existed.

The second sibling, now aged 7 years, had been born prematurely. The infant had been considered normal except for a defect in the external genitalia. A phallus of normal size was bound down ventrally and lacked a urethral meatus. Urine was emitted through a small opening at the base of the phallus. The normal-appearing scrotum contained palpable gonads. An abdominal exploration carried out in infancy revealed no female internal genitalia. The construction of a penile urethra was completed at the age of 6 years. At 7 years the boy was of normal height and weight. The penis was slightly hooded at the base with a fold of skin, but otherwise appeared normal except for old operative scars on the ventral surface. The scrotum contained small, very mobile gonads of normal consistency. This child also had a positive nuclear chromatin pattern in the buccal smears, and a urethrogram showed that there were no Müllerian vestiges. Studies of urine samples revealed a normal excretion of 17-ketosteroids and estrogens, a slightly elevated excretion of pregnanediol, and a gonadotropin excretion of less than 6 mouse units.

The scrotal contents were explored in both siblings. The testes of the postpuberal sibling showed seminiferous tubule dysgenesis which was identical to that found in Klinefelter's syndrome, whereas the testes of the prepuberal sibling were histologically normal. Sections of the 1-cm. oval mass from the upper pole of the right testis in the first sibling revealed ovarian tissue, consisting almost entirely of stromal elements in which a few scattered primordial and atretic follicles were identified. In the epididymis there was a tubular structure, lined by a pseudostratified columnar ciliated epithelium; this structure was presumably a vestigial fallopian tube. In the 7-year-old sibling a section of ovary sat cap-like on each testis. Within the ovary there was abundant stroma with numerous peripherally placed primordial follicles. Peripheral clumping of nuclear chromatin, characteristic of the female, was demonstrable in many Leydig cells in the testes of the first sibling and in the seminiferous tubule cells of the second sibling. As far as the authors know, this is the first reported instance of familial true hermaphrodism. In an addendum they call attention to a recent report on 2 siblings with true hermaphrodism in whom the chromatin pattern was negative.

Further Observations on Infection with Phage Type 80 Staphylococci in Australia. P. M. Rountree and M. A. Beard. M. J. Australia 2:789-795 (Dec. 13) 1958 [Sydney].

In 1953 a new phage type of Staphylococcus pyogenes var. aureus was isolated from infections of newborn infants in a Sydney maternity hospital. Later it was found that this particular strain, which had been given the phage type designation 80, had been responsible for a large proportion of outbreaks of neonatal infection in hospitals throughout Australia during 1954, and that it had become established as a cause of cross infection in adult patients at the Royal Prince Alfred Hospital, Sydney, where it had also caused an epidemic of boils in the staff. In 1955 and 1956 investigators found that the majority of penicillin-resistant staphylococci isolated from boils in Sydney belonged to this type. Apparently the same type of Staphylococcus organism was observed in Canada, and it was identified with phage type 81. The 2 phages, 80 and 81, are not identical, but their propagating strains are lysed by both phages and can be regarded as identical; their typing pattern is, therefore, 80/81. Other strains occur which are lysed only by phage 80 or only by phage 81, but these are much rarer. Strains of phage pattern 80/81 have been isolated in many parts of the world and have been responsible for much serious staphylococcic sepsis.

The authors report their observations during the 3 years that have elapsed since their first report. The data presented in this paper justify the view that much of the morbidity due to Staph. aureus occurring in Australia in the past 4 years has been caused by strains of phage type 80/81. Staphylococci of this phage type were responsible for 70 of 86 major outbreaks of staphylococcic infection among newborn infants in Australia from 1954 to the end of 1957. They predominated in serious infections in infants and older children admitted to children's hospitals in Sydney. At the Royal Prince Alfred Hospital since 1955 they have been the predominant, but not the only, staphylococci found in cross infection in patients, and they have been the chief cause of staphylococcic lesions in the nursing and medical staffs. Strains of this type are now widespread in communities outside the hospitals. A marked increase in the incidence of generalized staphylococcic infection in 1956 and 1957 was due almost entirely to them. In 9 out of 12 cases of fulminating staphylococcic pneumonia associated with Asian influenza in 1957, strains of this type were the infecting organisms. Nearly all the strains of this type are penicillin resistant, but so far resistance to other antibodies is more limited in extent.

Reaction of Lupus Erythematosus Serum with Nuclei of Circulating and Non-Circulating Cells. W. R. M. Alexander and J. J. R. Duthie. Brit. M. J. 2:1565-1566 (Dec. 27) 1958 [London].

Experiments carried out by other workers showed that tissue cells brought in contact with serum obtained from patients with disseminated lupus erythematosus and exposed subsequently to fluorescein-conjugated anti-human-globulin (Coombs's) serum showed specific nuclear fluorescence, thus providing strong evidence for the belief that the serum of patients with disseminated lupus erythematosus contains a globulin which combines with nuclei of tissue cells and leukocytes. The authors studied the serums obtained from 8 patients with disseminated lupus erythematosus and observed that nuclei of leukocytes from healthy persons showed the greatest affinity for the specific globulin. No evidence of uptake of globulin in tissue from patients with disseminated lupus erythematosus was found in vivo, but in vitro such tissue had less affinity for the specific globulin than tissue from healthy subjects. Nuclei of intact squamous epithelial cells pretreated with serum obtained from the patients with disseminated lupus erythematosus did not fluoresce on exposure to fluorescein-conjugated anti-human-globulin serum.

Cultivation of Human Breast Carcinomas. E. Y. Lasfargues and L. Ozzello. J. Nat. Cancer Inst. 21:1131-1148 (Dec.) 1958 [Washington, D. C.].

Although most of the human carcinomas have been successfully transplanted in vitro, the mammary carcinoma has remained a challenge for the investigator. The authors discuss some of the technical difficulties encountered in earlier reported attempts at explantation and growth of neoplastic tissues from human breasts. Recent progress in research on the mouse mammary carcinomas makes it imperative to grow human breast tumors for comparative studies. Since viral induction of these neoplasms in the mouse has gained more support, the availability of human tissue-culture material for experimental purposes could be enlightening, and valuable information might be obtained from its use in screening techniques for therapeutic agents.

The authors have developed a technique for the cultivation of human breast carcinoma cells, which in taking advantage of the weak intercellular bonds within the tumor harvests the cells "spilling" out of the tumor stroma when thin slices are cut with a razor blade. This suspension is sensitive to customary enzymatic concentrations which, therefore, cannot be used in the preliminary step of preparation. Agitation, even the slow motion of the roller drum, is unfavorable to the growth of the neoplastic cells; they have to be explanted in resting tubes.

Continuous cultivation of human breast carcinoma cells has thus been achieved for the first time. The cultures, derived from a mammary-duct-cell carcinoma of no special type, are now in their 6th month of life in vitro and are extremely proliferative. The regular growth rate of the neoplastic cells appears to be dependent on the presence in the medium of mucopolysaccharides introduced in the form of umbilical cord extract. Human placental serum and beef amniotic fluid, whose high content in estrogenic hormones is well known, also have a beneficial effect. Folic acid in a 2.5 mM.

concentration appears favorable to the growth of the cancer cells. However, a possible antagonism with cord extract has been considered in the spindle-shaped transformation which occurs in the epithelial cells when transferred from a folic acid medium to one enriched with umbilical cord extract.

The authors feel that the above-mentioned changes should be kept in mind in relation to the spindle-cell type of carcinomas occasionally observed by pathologists and to the spontaneous sarcomatous transformations of experimental carcinomas reported in the current literature. In an addendum they state that the fibroblast-like cells have again reverted to their original epithelial morphology. Such modifications, therefore, are determined by variations in the environmental factors and are reversible.

RADIOLOGY

Roentgenographic Study of the Progress of Osseous Metastases of Mammary Carcinoma After Bilateral Ovarioadrenalectomy. A. M. Dogliotti, A. Ruffo, F. Badellino and others. Minerva chir. 13:1213-1225 (Oct. 31) 1958 (In Italian) [Turin, Italy].

The authors report on roentgenologic findings of osseous metastases in 10 patients who underwent a bilateral ovarioadrenalectomy because of mammary carcinoma in an advanced phase. Eight patients died within a period of from 5 to 30 months after the operation. Improvement or deterioration of osseous metastases after operation was more tardily observed by roentgenograms than by clinical means. Cortisone therapy produced improvement in subjective symptoms and in state of health in only a few patients, although roentgenograms demonstrated severe lesions of osseous metastases. Roentgenograms and clinical findings may be dissimilar at particular periods of observation in these patients after operation, but the 2 methods complement each other in the over-all picture. Pictures of osteolytic foci and zones of recalcification, representing simultaneous processes of both bone destructive activities and of reossification, were observed in several patients. Clinical and biochemical findings determined which one of the 2 processes predominated. Periodic roentgenologic inspections of the whole skeleton can be used as a collateral, although tardy, procedure in evaluating the efficacy of bilateral ovarioadrenalectomy in patients with advanced mammary carcinoma. Laboratory investigation of calcemia and phosphatemia was a third procedure used in this series of patients. It can be particularly useful in discovering osseous metastases in those instances in which clinical and roentgenologic findings are negative. Simultaneous application of clinical, roentgenographic, and laboratory investigations seems to be the best method for observing the progress of osseous metastases in patients who have undergone bilateral ovarioadrenalectomy for advanced mammary carcinoma.

Thyroid Cancer in Youth. D. W. Petit, B. Catz and P. Starr. California Med. 89:394-396 (Dec.) 1958 [San Francisco].

The authors report on 9 boys and 2 girls with cancer of the thyroid, whose ages ranged from 5 to 18 years at the time the diagnosis was made. In 8 of the 11 patients the diagnosis was suggested by persistent enlargement of the cervical lymph nodes. Seven patients were subjected to total thyroidectomy, 3 underwent hemithyroidectomy, and 1 had repeated removal of lymph nodes in the neck, only one of which was cancerous. After total ablation of normal thyroid tissue and removal of as much malignant tissue as possible surgically, scintigram and/or radioautograph studies with radioiodine (I^{131}), administered in doses of 1/10th to 10 mc., were carried out in 9 of the 11 patients. In 6 of the 9 patients uptake of the radioactive material was demonstrated. These 6 patients then were treated with I^{131}, a dose of 100 mc. being given by mouth. Administration of the radioactive agent was continued, with interval studies in which millicurie doses were used for tracer purposes only until no further uptake was observed. During this whole period the patients were kept in a euthyroid state by the administration of thyroid hormone or levothyroxine. The patients were followed up for periods ranging from 10 months to 9 years. Of the 11 patients, 9 were free of metastases as nearly as could be determined. One patient had metastatic pulmonary lesions that were not shown to take up I^{131} and that progressed despite the administration of a total dose of 250 mc. of I^{131}. Another patient had questionable pulmonary metastasis.

Nine of the 11 patients had had roentgenotherapy to the head or neck previous to the diagnosis of thyroid cancer. Other workers had reached the tentative conclusion that irradiation is possibly carcinogenic to the normal preadolescent when given in therapeutic amounts. In 2 previously reported series of thyroid cancer in children, 10 of 28 patients in one and 15 of 15 patients in the other had had roentgen-ray treatment to the head and neck before the cancer was diagnosed. As yet, there have been no surveys that would establish the incidence of head-and-neck irradiation in a population of the kind represented by the authors' patients, but the significance of the reported observations would depend on the incidence. Inasmuch as the ultimate answer to the problem of such irradiation as a possible stimulus to the production of thyroid cancer is not yet at hand, it would seem prudent to avoid, if possible, therapeutic irradiation to the head and neck of preadolescent children with a normal thyroid gland.

Operative Cholangiography in the Diagnosis of Prolonged Jaundice in Infancy. J. H. Harris Jr., A. E. O'Hara and C. E. Koop. Radiology 71:806-815 (Dec.) 1958 [Syracuse, N. Y.].

Whereas in many institutions operative cholangiography is a routine procedure during biliary tract surgery in adult patients, the value of delineating the biliary ductal system in pediatric surgery is not generally realized. The authors describe the technique of operative cholangiography that is being used at the Children's Hospital of Philadelphia. The peritoneal cavity is entered through a small right subcostal incision, and the gallbladder is identified. If the latter is of normal size and contains normal appearing bile, a patent communication between the gallbladder and the liver may be assumed, but this does not reflect the caliber of the communication. Furthermore, this does not aid in the differentiation between the "inspissated bile syndrome," viral hepatitis, and atresia of the common bile duct. A mushroom catheter is inserted into the gallbladder through a small cholecystostomy, and held in place with a purse-string suture. After irrigation of the biliary ductal system to eliminate artefacts caused by bile plugs, 8 to 20 cc. of 15% Urokon is injected through the catheter. It is important that the patient be apneic during the x-ray exposure, and that the exposure be made after approximately 80 to 85% of the contrast medium has been introduced. The authors attempt to obtain a right posterior oblique projection in order to avoid superimposition of the ductal structures and to project them away from the spinal column. If the cholangiographic findings indicate a normal biliary ductal system with free flow of the contrast medium into the duodenum, a liver specimen is taken for biopsy, and the abdomen is closed. If, on the other hand, there is roentgenologic evidence of atresia of the ductal system, the initial incision is extended to allow adequate exposure for exploration of the porta of the liver.

Since 1953 operative cholangiography has been employed in 12 instances. Three infants were 1 month of age; the oldest child was 21 months old. Of the 12 patients, 6 were found to have normal extrahepatic ductal systems, 1 had atresia of the common bile duct, and 4 had congenital atresia of the hepatic ducts. The histories of 4 of the children are described in detail. In one of these no contrast medium was seen in the common hepatic duct or its radicals, and the roentgenogram was interpreted as representing atresia of this portion of the ductal system. However, when the cholecystostomy was done, normal bile was found in the gallbladder, and because of this the roentgenologic findings were considered to be falsely indicative of biliary atresia. The liver biopsy specimen, taken at the time of laparotomy, revealed hepatitis. In each of the other 11 cases, the operative cholangiographic findings helped the surgeon. When a normal biliary tree was outlined, the abdomen was closed. The surgical procedure was thereby shortened, reducing both the surgical trauma and the exposure of the already embarrassed liver to anesthetic agents. In addition, since only the gallbladder was involved in the surgical dissection, the possibility of postoperative fibrosis about the normal infantile ducts was avoided.

The causes of jaundice in newborn and older infants are icterus neonatorum, congenital hemolytic jaundice, erythroblastosis fetalis, syphilitic hepatitis, jaundice due to sepsis, intrauterine viral hepatitis, and congenital atresia of the bile ducts. Uncorrected atresia of the bile ducts is not compatible with long life, although many patients survive for some years. The early clinical picture is that of a jaundiced child with dark urine and acholic stools. Recent work tends to implicate the virus of homologous serum hepatitis in acquired biliary atresia. The fact that biliary atresia is the most frequent cause of obstructive jaundice in infancy, that in its unaltered course the disease is fatal, and that only early surgical correction can prevent the cirrhotic process emphasizes the importance of early limited exploration and study of the biliary ductal system by operative cholangiography.

Undulant Fever Spondylitis. F. Zammit. Brit. J. Radiol. 31:683-690 (Dec.) 1958 [London].

Undulant fever caused by Brucella melitensis is endemic in Malta and causes much disability. Diagnosis is difficult during its early stages. The blood should be tested for the agglutination reaction. A serum agglutination reaction of 1:80 is regarded as diagnostic, but in some cases the reaction does not rise above 1:40. A rising titer is indicative of active brucellosis. Blood culture is not always positive. Bone marrow examination may help in the diagnosis, especially when it is drawn from the sites which show roentgenologic signs of bone involvement. The main symptom of this disease is a highly irregular fever, with the temperature rising and falling, which goes on for long periods and is often associated with headaches, enlargement of the spleen, excessive perspiration, secondary anemia, weakness, and pains of a rheumatic type. The commonest sites of these rheumatic pains are the neck, shoulder, lumbar region, hip, thigh, and knees.

The author reviewed all the cases diagnosed as brucellar spondylitis in the orthopedic department of a hospital in Malta from 1947 to 1954. During this period spondylitis was diagnosed in 115 of 6,301 patients with undulant fever. In a typical case the signs and symptoms of spondylitis manifested themselves during the period of convalescence from brucellosis. The earliest and most constant symptom was pain, localized to the affected region of the spine. It was made worse by movements and was relieved by rest. Referred pains to the limbs, and in some cases the girdle type, occurred. Spasm of the spinal muscles was commonly present. In 62 of the patients roentgenologic evidence of spine involvement was found; the regional distribution was as follows: cervical, 5; thoracic, 16; combined thoracic and lumbar, 4; and lumbar, 37. The 4th lumbar vertebra was most commonly involved. The main changes were destructive lesions in the vertebral bodies, usually marginal, with characteristic sclerotic reactions around them and proliferative marginal new bone formations resembling calcifications of ligaments or osteophytic processes. The disk space was usually narrowed. Signs of cord compression were present in 8 patients. The following conditions have to be differentiated from brucellar spondylitis: Pott's disease, staphylococcic osteomylitis, actinomycosis, osteochondrosis of the vertebrae, and osteoarthritis.

Treatment is largely conservative; in recent years antibiotics have been administered with favorable results. The author found that most patients derived benefit from rest in bed or on a Bradford frame. When root pains, with radiation to the upper and lower limbs, were present, traction was applied, and the patient was eventually relieved. When the condition of the patient improved and the pain abated or disappeared, a plaster jacket was applied. Recovery took place after several months, depending on the extent of the lesion, and in the majority of cases the patient returned to his former work. The period of disability varied from 3 to 6 months in 60% of the patients; in the rest, in whom the lesion was more extensive, it lasted longer.

PUBLIC HEALTH

Effect of Ingestion of Distilled Spirits on Automobile Driving Skill. B. B. Coldwell, D. W. Penner, H. W. Smith and others. Quart. J. Stud. Alcohol 19:590-616 (Dec.) 1958 [New Haven, Conn.]

The authors carried out practical road tests on 50 experienced automobile drivers who consumed known amounts of distilled spirits. Under the given experimental conditions, the impairment of driving skill was definitely evident in one subject in whom the venous blood alcohol level was 0.036%. Signs of impairment were observed in 5 out of 7 subjects whose venous blood alcohol levels at the time of driving did not exceed 0.05%. Heavy drinkers showed less impairment of driving performance than light drinkers with the same blood alcohol levels, but signs of impaired driving ability were exhibited by 8 out of 10 heavy drinkers with venous blood alcohol levels ranging from 0.051 to 0.12%. Not one subject in whom the blood alcohol level was around 0.15% was able to maintain his driving ability as shown before drinking. Twenty-five drivers manifested significant impairment of their driving abilities when their venous blood alcohol level was 0.078%. The impaired ability in handling cars, such as manipulation of clutch, brake, gearshift, and accelerator, even at a relatively low venous blood alcohol level, was the most striking feature in the tests, in contrast to the drivers' skill to avoid stanchions. The experimental driving situation favored the subjects; therefore, one may assume that the influence of alcohol would be more pronounced on the driving performance in urban areas than on that observed in the tests.

Vaccination Against Poliomyelitis with Living Avirulent Viruses: Preliminary Report. F. Buser and M. Schär. Schweiz, med. Wchnschr. 88:1282-1284 (Dec. 20) 1958 (In German) [Basel, Switzerland].

Killed or living viruses of attenuated virulence are required for active immunization against poliomyelitis. Salk vaccine belongs to the first group; it contains strains of 3 types of poliomyelitis virus inactivated with formaldehyde. Since the Salk vaccine has been used in about 100 million persons and has given protection against the paralytic form of poliomyelitis, it may seem superfluous that immunization experiments are still being carried out with avirulent poliomyelitis viruses. However, test immunizations with living viruses date back to 1950, whereas "field trials" with the Salk vaccine were not begun until 1954. Both types of immunization have their advantages and disadvantages. Simultaneous immunization against all 3 types of poliomyelitis and absence of excretion of virus are some of the advantages of the killed virus vaccine of the Salk type. Oral administration, good and prolonged immunity, and absence of allergic reactions are advantages of immunization with the living avirulent virus.

The authors felt that the advantages of immuniza- with living viruses justified further vaccination experiments under clinical, virologic, and serologic control. They administered the attenuated type 1 poliomyelitis virus of H. Koprowski, known as the "Chat-Strain," by mouth to 115 persons (40 adults, 46 children, and 29 infants). The immunization produced no symptoms in any of these persons, and no case of poliomyelitis was observed during the immunization and for 3 months thereafter in the locality where the test persons resided. Poliomyelitis virus was demonstrated in the stools on the 10th day in 90% of the vaccinated infants and children and in 45% of the adults. Fifty-eight of 60 persons who had no antibodies against poliomyelitis virus, type 1, before the oral immunization showed a titer increase to 1:50 and higher. Only 2 adults showed no measurable increase in antibodies.

BOOK REVIEWS

Treatment of Cancer and Allied Diseases. Volume I: Principles of Treatment. By fifty-five authors. Edited by George T. Pack, M.D., F.A.C.S., Attending Surgeon, Memorial Center for Cancer and Allied Diseases, New York, and Irving M. Ariel, M.D., F.A.C.S., Associate Clinical Professor of Surgery and Associate Attending Surgeon, New York Medical College, Flower and Fifth Avenue Hospitals, New York. [To be in nine volumes.] Second edition. Cloth. $22.50. Pp. 646, with 505 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This is the first of nine volumes to be published. The other eight are to be concerned with specific neoplasms according to their origin in anatomic areas or systems. The first edition was in two volumes of such size as to be read only at a sturdy desk or table; the present volume is considerably smaller than the earlier books but still too heavy for armchair use or for reading in bed. Fifty-five authors have contributed to this volume alone, to accomplish a general review of organization (clinics and home care), diagnosis and pathology, some features of surgical therapy, methods of irradiation (5 of 10 section are devoted to this), hormonal treatment, chemotherapy, care of incurables, and reporting of end-results.

It is obvious that in the 37 chapters there is much important information although the overlapping, the conflicts of opinion, and the rapid obsolescence common to all such encyclopedic efforts are apparent here. Subjects which are presented in a superior fashion in the opinion of this reviewer include biopsy diagnosis, exfoliative cytology, electrosurgical treatment, radiosensitivity, the physical basis of radiation therapy, chemotherapy, and the reporting of end-results. The last-named section provides clear, practical guidance on the "why" and "how" of pertinent statistical methods. In a chapter on care of the patient before and after operation Ariel and Pack present a scholarly review of the problems in the biochemical and metabolic changes that follow the operative treatment of cancer. There is room for doubt that the practicing surgeon's basic knowledge will be enlarged significantly thereby, but the neophyte should be acquiring such information as part of his formal training.

Although there are advantages in low-voltage, short-distance (*sic*) x-ray treatment of surface lesions, the measurement of tumor dose by the "D½" or any other method is tricky, and much of the information presented in this connection is unconvincing. An important section on current palliative treatment by hormonal methods unhappily is poorly organized, frequently repetitious, and sometimes inaccurate. Written by one of the pioneers in the androgenic therapy of mammary carcinoma, this section shows a strong bias for androgens and perpetuates some of the myths which persist regarding this type of treatment. These errors include a belief that androgens given for two months after oophorectomy will hasten the regression of disease, that androgens are superior in skeletal metastasis at any age, that 30% of all patients obtain regression with androgens, and that after regression does occur the hormone employed should be discontinued. Each of these statements is inconsistent with more recent reports of various authors, and in particular with the data reported periodically during the past decade—and this year in final conclusions on 580 androgen-treated and 364 estrogen-treated patients—by the Subcommittee on Breast and Genital Cancer, Committee on Research, American Medical Association. The latter report confirms the conclusions of various investigators, since rates of regression for metastasis in bone of 24% with androgens are equaled by 27% for estrogens, while in all other situations by age, site of lesions, and time of recurrence, estrogens are either equal or superior to androgens in women four or more years postmenopausal. Other inaccuracies in this chapter are an apparent confusion of 'fibroadenoma' with dysplastic adenosis, an expression of the invalid taboo against substitutional use of estrogens for genuinely severe menopausal symptoms in women previously treated for breast cancer, a failure to emphasize the dominant role of orchiectomy in prostatic carcinoma, and a tacit approval of adrenalectomy for the latter neoplasm. Perhaps a clue to the unsatisfactory state of this section is found in the 141 references listed; divided by five-year intervals beginning in 1946, 52 of the bibliographic items were published prior to 1946, 41 and 43 in the next two five-year periods, and only 5 in 1956 or later. A single area so deficient must dampen one's admiration for the whole. The penalty for the lapse of time from manuscript to book is particularly evident in connection with methotrexate, triethylene melamine, triethylene thiophosphoramide (Thio-Tepa), nitrogen mustard, Methadone hydrochloride, and pantopon hydrochloride.

This is still a valuable reference source for libraries. The physical features of the book are beyond criticism. The index is detailed, and there are for all chapters reference lists of some length, inconveniently massed at the back of the book. Noted on page 609 is the most entertaining title since megavoltage units first made headlines (chapter 18, 12). It concerns the application of "Sugar-Hard X-Rays," but seems to give too little credit to the source, which is the first 1-Mev unit developed by Mudd at the California Institute of Technology.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

HISTAMINIC CEPHALALGIA

To the Editor:—*A 56-year-old man who has had histaminic cephalalgia for 10 years has shown only fair response to a course of histaminic desensitization with an ergotamine and caffeine preparation, aspirin, ACTH, and orally given steroids. What other treatment should be tried?*

Alexander Wallace III, M.D., Los Angeles.

Answer.—In a recent article, entitled "Histamine Cephalalgia and Its Relation to Migraine" (*Ann. Allergy* 16:300, 1958), Unger concluded that histaminic cephalalgia is characterized by attacks of excruciating unilateral facial pain, inflammation of the eye, and rhinorrhea or blocking of the nose on that side; one of his patients was relieved by abstinence from pork, another by abstinence from milk, and a third by removal of infected teeth; migraine headache was also present in two of these three patients; histaminic cephalalgia and migraine headache are probably closely related; although histamine injections usually give good results, this does not prove that elaboration of histamine at the site of the pain causes the symptoms; and the theory that injections of histamine lead to desensitization is likewise not proved. A thorough search should be made for a focus of infection, especially dead or abscessed teeth or infected tonsils, and elimination diets, beginning with one from which milk, pork, and chocolate are rigidly excluded, should be followed for about two weeks. Then, if there is no relief, new diets should be tried, e. g., one which excludes wheat and other cereals and then one with avoidance of meat, fish, fruits, and vegetables, in succession.

GENERAL ANESTHETIC FOR A CHILD

To the Editor:—*Is there any type of general anesthetic which a pediatrician may use without risk to the patient in the performance of such minor operations as sutures of skin wounds, abscess drainage, and reduction of fractures or luxations?*

Juan Silverio, M.D., Marianao, Cuba.

Answer.—There is no type of general anesthetic that may be used without risk to the patient, no matter how minor the operative procedure is. The risk of anesthesia involved in outpatient procedures is greater than most, because patients are excited and often have quantities of undigested food in their stomachs. These two factors add such danger to the average risk of anesthesia that experienced anesthetists regard such cases as especially hazardous. Unless carefully managed, such patients struggle and resist anesthetic induction and later may aspirate vomitus and die. Such tragic accidents occur with alarming frequency throughout the United States. How then, does one treat children who require minor emergency operations? When possible, it is wise to allow an experienced anesthetist to assume the responsibility. Often a pediatrician or practitioner must act for himself, however. In such cases, he should definitely avoid the hazards involved in attempting both to anesthetize his patient and to perform the operation. There are several alternatives. At the outset, one should take time to quiet the child with a mild sedative which will calm but not depress him. Pentobarbital, or a relatively small dose (0.5 mg. per year of age) of morphine, is effective. Time must be allowed for such a drug to act. An understanding physician can accomplish a great deal by reassuring the child and gaining his confidence.

If, after this preparation, the physician uses local infiltration anesthesia, he will be able to take care of most minor lacerations and similar injuries. Ethyl chloride spray may be used if abscesses are to be opened. If a Colles' fracture is to be reduced, the fracture site may be infiltrated with a 1% solution of procaine or the fracture may be adroitly reduced without anesthesia. These measures fall short of the ideal, but they are definitely safer than would be the use of a general anesthetic by an untrained person. In many areas, a pediatrician may obtain enough training in anesthesia to justify his use of short-acting agents, such as vinyl ether, which has definite advantages for minor operations. This agent, however, may cause severe convulsions and hypoxia, or toxic liver necrosis, and consequently should not be used by trial and error methods.

ADRENOCORTICAL STEROIDS

To the Editor:—*Is there any indication for or any adequate proof of the advantage of adrenocortical extract over the various synthetic adrenal steroids (prednisone or ACTH) in the treatment of any condition? Please comment on the use of adrenocortical extract in chronic congestive heart failure, presumably refractory to routine therapy; it has been said that, in this condition, adrenocortical extract has advantages over ACTH.*

Warren F. Wilhelm, M.D., Kansas City, Mo.

Answer.—Adrenocortical extract is theoretically a composite of the steroids found in the adrenal cortex and so should have multiple effects. For practical purposes, however, it resembles desoxy-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

corticosterone acetate in its action; that is, it is more like the mineralocorticoids than the glucocorticoids. Such synthetic adrenal steroids as prednisone and ACTH have primarily a glucocorticoid effect. Therefore, adrenocortical extract would be preferable in those situations requiring a mineralocorticoid effect, for example, in acute adrenal insufficiency, where a low serum sodium level and a low extracellular fluid volume are the immediate concerns. In regard to chronic congestive heart failure refractory to routine therapy, one must first decide whether steroids of any kind are indicated. This class of drugs has until recently been considered contraindicated in congestive heart failure because of salt and fluid retention, which may be a serious matter. In recent years, however, some apparently paradoxical effects of steroids in inducing diuresis have been observed in patients with intractable congestive heart failure. The exact mechanism of this diuresis remains to be elucidated. Various data suggest that renal tubular reabsorptive mechanisms may be involved, antidiuretic hormone activity may be inhibited, and/or aldosterone may be influenced. As long as the exact physiological explanation for the ability of steroids to cause an increase in urinary output under certain circumstances remains undetermined, it is difficult to state whether ACTH or adrenocortical extract would theoretically be more effective. Although both have been used, in most of the reported studies ACTH, cortisone, or other agents primarily glucocorticoid have been administered preponderantly. For this reason and because adrenocortical extract is extremely expensive and relatively less available, ACTH would seem preferable should one believe that the steroids are worthy of trial in severe congestive heart failure.

EXTREME LONGEVITY

To THE EDITOR:—*A man in a nearby place claims to be 185 years old. There are no records to substantiate his statement. Is any method available to gain at least an approximate estimate of his age? Is the technique of using carbon-14 or any other test applicable in this regard, for example, a test on dental enamel? All other tissues of the body are renewed too often to supply desired information.*

Manouchehr Gueramy, M.D., Shiraz, Iran.

ANSWER.—No chemical or anatomic methods are available to determine an adult's age. The use of carbon-14 is not practicable, because the turnover of carbon in the body is too rapid. In other words, the test is of little value in determining the age of living substances. In addition, the accuracy of the carbon-14 test on inert objects varies up to 150 years one way or the other.

PINWORMS

To THE EDITOR:—*A patient has had a persistent pinworm infestation. She was exposed to them by her child seven years ago. Since then, she has had many courses of treatment. Although all the accepted drugs have been used and her home technique made sure of, she still has a recurrence every 6 or 7 months after apparently being cured. The standard treatment, including mercurial ointment, enemas, a drug by mouth (piperazine tartrate, gentian violet, oxytetracycline, and other agents), and appropriate care of the hands and linen, has been used many times. She is an intelligent, extremely neat person. The children have been rechecked regularly and no worms have been noted since the first attack seven years ago. What can be done for this patient?*

M.D., New York.

ANSWER.—Since the children in the family have not had pinworms since their first attack and since the mother is described as an extremely neat person, the diagnosis of enterobiasis is questionable. Is she a compulsive, highly literate woman who may be upset by the problem and who keeps imagining infection? Mothers have been seen who become severely upset about pinworm infestation and describe "worms" that do not exist. The diagnosis should be checked carefully by Scotch-tape smears taken before bathing. A series of smears should be made on three consecutive mornings, and if these show negative findings she should be firmly assured that no worms are present and told to stop looking for them. There are no carriers of pinworms. This common intestinal parasite of children does not infect household pets, as is commonly suspected.

ANSWER.—It is probable that the continued source of reinfection is in the home and that one or more other members of the family harbor asymptomatic infections. The simplest and most logical procedure to follow in this case would be to simultaneously treat all members of the family with piperazine, using a dosage of 50 mg. per kilogram of body weight per day, but not exceeding 3 Gm. per day, for eight consecutive days. The best results have followed the administration of the total daily dose, at one time, about two hours before breakfast.

ANSWER.—The ubiquitous pinworm, Enterobius vermicularis, evades all sanitary barriers and invades all classes of society. It is the most common parasitic worm of civilized man. Its peculiar, brief life cycle, lasting two to six weeks (seldom three months or longer), makes infection and reinfection sure and prompt. Eggs, when ingested, hatch in the small intestine and worms occur in various stages of development from the ileum, cecum, and appendix through the colon and rectum. There is no deposition of eggs in the lumen of the host's intestine. The gravid females, when ready to oviposit, swarm into the rectum, usually at night. They wriggle out of the anus, causing pruritus or rectal pain. The consequent rubbing and scratching of the affected parts results in crushing the worms and smearing many thousands of embryonated eggs into the perianal area. Eggs soon mature on exposure to air and become infective. Thus, fingers, underwear, night clothes, and bed sheets create a risk of continuous or interrupted reinfection with eggs which is greater for the infested person than for others. Finger transmission of eggs from anus to mouth is the principal mode of massive or cumulative infection. Some larvae, emerging in the moist surroundings of the anus, may enter the intestine by the anal route. Eggs dislodged from the host's perianal region become widely disseminated in the house. Airborne infection with dried eggs from room dust via the mouth and nose results in chronic light infections. These singular modes of infection might help to explain the peculiarities of the case presented.

Although perianal itching at the time of the emergence of gravid females from the anus is a frequent occurrence, many adults and children harboring pinworms experience little or no pruritus and, therefore, are not conscious of infection. Pinworm infection has been discovered by the Scotch-tape anal swab technique in many unsuspecting parents of already infected children. Such persons may be justifiably regarded as the carriers of infection. There are, on the other hand, others who suffer severe pruritus from even light infections with pinworms. They probably have become allergic to the worms or their products.

The following procedures are recommended for prophylaxis and treatment: 1. All members of the household should be examined or reexamined, including the husband and servants, by the Scotch-tape swab technique. The swabs should be done early in the morning, before a bath; a series of seven should be taken on alternate mornings and especially any morning after a night when itching has occurred. All those found to be infected should be treated simultaneously. 2. The patients should be cautioned to wash hands before eating and smoking. 3. They should be told to change bed sheets, underwear, nightgowns, and similar items daily. The bed sheets should not be shaken but removed gently and laundered after each use. The rugs, curtains, sofas, chairs, and table-tops should be vacuum-cleaned once a week. 4. Before retiring at night, the patient should place a liberal amount of 5% ammoniated mercury ointment on a piece of polyethylene plastic sheet and apply it to the perianal area, holding it in place with a sanitary napkin. The patient should remove and discard it the next morning in the bathroom and take a shower, thoroughly washing the perianal area with soap and water. Freshly laundered underwear should then be put on. 5. The bathtub, toilet seat, the bathroom floor, and fixtures should be wiped with 2% saponated cresol solution.

Two new and usually effective therapeutic agents are now available: Dithiazanine, a cyanine dye, is supplied in the form of 0.1 Gm. tablets, and the adult dosage is 200 mg. (two tablets) three times daily for five consecutive days (Schwartzwelder and others, *J. A. M. A.* 165:2063-2067 [Dec. 21] 1957). Pyrvinium chloride, also a cyanine dye, marketed as a strawberry-flavored suspension, is given in a dosage of 2 mg. per kilogram of body weight per day, in two equal doses daily for six consecutive days (*Am. J. Trop. Med. & Hyg.* 7:212, 1958).

RECURRENT PHLEBITIS

To the Editor:—*Over the past five years, a married woman has suffered at intervals of months or years from attacks of phlebitis involving her legs from ankle to groin (three times on the right and twice on the left). Once she suffered a pulmonary embolus. On two occasions she was in Seattle, Wash., once in Long Beach, Calif., and twice here in Mexico, and everywhere physicians have been at a loss as to the cause. Treatment has included rest, hot packs, antibiotics, and anticoagulants. Attacks have lasted one to eight weeks. Please suggest a course of treatment.*

Richard H. Lyon, M.D., Jalisco, Mexico.

Answer.—This patient seems to be suffering from recurring infectious thrombophlebitis with lymphedema. The original cause is not known, but such patients are likely to develop recurring episodes with chills and fever, precipitated by mild trauma or any systemic infection, however mild. This is particularly true with recurring upper respiratory infections. In addition to rest in bed, continuous warm wet compresses over the limb, elevation of the foot of the bed, antibiotics, and anticoagulants, methacholine chloride, administered by iontophoresis every other day for a series of 10 treatments, and use of an oscillating bed are often helpful. These measures should improve the venous circulation and help overcome spasm of both the veins and arteries. Vasodilators are usually prescribed, such as nylidrin (6 mg. given three times a day before meals) and papaverine hydrochloride (60 mg. given after meals and at bedtime). In chronic cases, when there is evidence of an active perivenous inflammation, trypsin therapy (2.5 mg. given twice daily for 10 days) is helpful. The condition usually is reasonably controlled in two or three weeks. The important thing is to continue the treatment for a prolonged or indefinite period. The patient should wear an elastic support for at least three months. Anticoagulant therapy should be continued for at least six months but should be properly supervised with prothrombin time estimations. Another suggestion which may be applicable here would be to continue the antibiotic therapy, particularly if the source of infection is determined. Sometimes it may be in the sinuses, throat, or urinary tract. In such cases 200,000 units of penicillin and 500 mg. of a triple sulfonamide, such as sulfadiazine, sulfamerazine, and sulfamethazine, may be given daily for a prolonged period. This measure may be helpful in preventing recurrences.

Reference

Kramer, D. W., and de Medeiros, A.: Medical Management of Thrombophlebitis and Postphlebitic Syndrome: Survey of 400 Treated Cases from Series of 779 Consecutive Cases of Phlebitis, J. A. M. A. **165:**767-773 (Oct. 19) 1957.

PAIN IN LOWER EXTREMITY

To the Editor:—*A man, aged 47, who works actively every day complains of pain in the left lower extremity. It began suddenly seven years ago while he was walking down a steep hill. The pain in his left hip, thigh, and calf at that time was so severe he could not bear weight on the left side. He spent the next hour or so working himself up to the point of being able to walk again after sliding down the hill the rest of the way and walking to the car. Then he recovered completely, but ever since then, whenever he walks 100 yards quickly, a sudden pain in the thigh and calf stops him "dead" and he has to take the weight off the left lower extremity and rotate it inward and outward at the hip, which relieves it within five minutes. Then he is perfectly all right, with no residuals. He has tried sitting down when the pain strikes him, but that does not help. If he is walking more slowly the pain comes gradually but is treated the same way, and if he walks slowly enough he can walk all day without pain. At worst the calf will cramp; otherwise, there is a deep-seated pain in the whole thigh and leg which he cannot localize because there is no tenderness. A few times the foot has tingled slightly. There is no subjective skin temperature or skin color change. Pulsations in the dorsalis pedis artery are good. There is never any swelling or trophic change. Five or six physicians, including a specialist, have examined him. Please suggest treatment.*

Robert S. Hamilton, M.D., Conrad, Mont.

Answer.—From the history, it is presumed that the circulatory function studies have given normal results. It is possible that this patient may have arteriospasm with a claudication-like pain at times. He may have some marked irritation of the posterior nerve roots. This may have been a sacroiliac condition at the onset or, more likely, a disk syndrome. Walking down the hill may have set off some pathological changes of the ligaments around the spine, which permitted some injury to the spine or slipping of an intervertebral disk. It is also possible that the disk may slip in and out at times and may produce marked symptoms alternating with times when patient is symptom-free. This patient should be thoroughly x-rayed in reference to some spinal injury with either a neurosurgeon or an orthopedist supervising the studies. A myelogram may throw some light on this case and would enable any pathological findings to be corrected. In the meantime, the patient should be treated with analgesics and vasodilators to overcome the arteriospasm. Further investigation should be carried out to arrive at the source and attempts made to correct the offending factor.

CHLOROTHIAZIDE AND OLIGOHYDRAMNIOS

To the Editor:—*An 18-year-old primigravida was recently delivered at term of a girl weighing 6 lb. 2 oz. (2,800 Gm.) and showing bilateral marked talipes varus but no obvious bony abnormalities. Oligohydramnios seemed to be present. During the last six weeks of pregnancy the patient was almost continuously on therapy with chlorothiazide because of excessive weight gain (25 lb. [11.3 kg.] in four weeks) and pitting edema, with a rise in blood pressure from 120/70 to 160/90 mm. Hg in the same four weeks. No albuminuria was found. With use of this drug, the patient lost 14 lb. (6.4 kg.). What is the influence of chlorothiazide on amniotic fluid, since the oligohydramnios appears to be a causal factor in the development of the clubfeet?*

M.D., Virginia.

Answer.—A number of drugs having carbonic anhydrase inhibitory activity have been used in an effort to effect a reversal of the sodium and water retention characteristic of the late toxemias of pregnancy. Of these drugs, chlorothiazide seems to be one of the most effective. The effectiveness of this type of therapy will be apparent clinically by a rapid weight loss, a diminution in edema, and occasionally a reduction in the tone and size of the uterus. The latter is especially apparent when polyhydramnios has been present. Frequent circumferential measurements will provide the best evidence of a diminishing volume of amniotic fluid. The relationship between oligohydramnios and the presence of skeletal or muscular abnormalities in the fetus, such as talipes varus, is obscure. Skeletal and muscular defects occur frequently in an abdominal pregnancy where there may be no amniotic fluid protection. On the other hand, many similar defects have been observed in premature infants and aborted fetuses when no constriction or abnormal pressure factors seemed to be present. It would seem most unlikely that the bilateral talipes varus present in the infant described was the result of the use of chlorothiazide. Although this possibility cannot be absolutely excluded, it should be borne in mind that the hazards incident to the inadequate treatment of preeclampsia may be exceedingly great. Certainly, the active treatment of preeclampsia should be the primary objective.

COAGULATION TEST

To the Editor:—*Years ago a blood clotting test, known as the coagulation valence, was described by Fonio. The basis of the test is the ability of blood to clot when mixed with a substance which inhibits coagulation, in this case magnesium sulfate. What is the anticoagulant mechanism of magnesium sulfate, which is evident even with low dilutions of this salt? What clotting factor or factors in the blood is removed by it?* *J. H. Rogers, M.D., Gadsden, Ala.*

Answer.—Magnesium sulfate, as well as other salts of magnesium, depresses coagulation. High concentrations of calcium salts and even sodium chloride also effect an inhibitory action of coagulation. It is likely that this is a nonspecific effect and probably is not specific for magnesium. This consultant is unaware of any recent work that has been done to determine in what phase of the clotting mechanism these inorganic salts act. The older literature is noninformative, because the various clotting factors were not differentiated until recently.

Answer.—Although much work has been done on the relationship of certain cations, particularly calcium and other alkaline earth elements, to the coagulation mechanism, there is still much ignorance regarding the precise clotting factors on which they act. Interest in this area has recently been reawakened in the light of our newer knowledge of the coagulation sequence. The following information regarding the mechanism by which magnesium sulfate may act as an anticoagulant is largely derived from early work of Stefanini and Quick (*Am. J. Physiol.* 152:389, 1948), who made studies on blood decalcified by an ion exchange resin (Amberlite). It was demonstrated that calcium is both a procoagulant as well as an anticoagulant, depending on the concentration used when re-added to the decalcified plasma. This has been recently reconfirmed with highly purified materials, demonstrating the quantitative relationships required for the biological activation of highly purified prothrombin (Goldstein, Izak, and Zonderman, *Fed. Proc.* 16:48, 1957; Alexander, in Transactions of the Fourth International Congress of Biochemistry, New York, Pergamon Press, 1958, to be published).

DYSPNEA AND ABDOMINAL DISTENTION

To the Editor:—*A 76-year-old woman performed such heavy work as pitching hay until two years ago. Her only complaint was dyspnea easily relieved by stopping work for a few minutes. About 10 years ago a 25-lb. growth (probably an ovarian cyst) was removed from her abdomen through a midline incision. She has had a "big stomach" ever since. All other findings are normal, except for a marked meteorism; her abdominal walls are felt to be under great pressure. This condition has been present since her operation. Palpation is unsatisfactory, but there is no indication of mass or free fluid. Although she has dyspnea, she can touch the floor easily when bending over with her knees straight. What might cause such a condition? Would it be safe to give a trial dose of neostigmine?* *M.D., New York.*

Answer.—The meteorism which was noted by the examining physician might well contribute to this patient's dyspnea, but one would have to attribute it mostly to the arteriosclerotic heart disease which must be present. The enlargement of the abdomen may be due to many causes, but the three most obvious, in view of the patient's history, are recurrent tumor, ascites, or intestinal distention. In view of the time since her operation and the absence of masses or free fluid, the sole cause must be a distended colon. The colon is probably dilated, secondary to a functional or organic partial obstruction in the lower sigmoid or rectosigmoid. A functional obstruction may be due to degeneration of the myenteric plexus caused by nutritional deficiency. Partial organic obstruction could be produced by diverticulitis, operative adhesions, or a chronic twisting or kinking as the sigmoid enters the pelvis. The diagnosis will depend on sigmoidoscopy, roentgenograms of the abdomen, and a barium enema. If these studies demonstrate a functional obstruction (acquired megacolon) it may be controlled by enemas and saline solution laxatives. The various choline derivatives have not proved satisfactory in such older patients because of their cardiovascular side-effects.

CARBON MONOXIDE AND CORONARY INFARCTION

To the Editor:—*Could a few whiffs of fumes from an automobile exhaust precipitate a coronary infarction? A 65-year-old man inhaled such fumes and within 15 minutes developed an acute coronary occlusion.* *M.D., Illinois.*

Answer.—The question implies a very brief exposure to automobile exhaust gas, and it can be assumed that this exposure was not followed by any long period of unconsciousness due to deprivation of oxygen. It is highly improbable that there could be any connection between the exposure described and the appearance of the coronary accident. Automobile exhaust gas does have other components than carbon monoxide, usually small amounts of hydrocarbons, but the effect of these contaminants on the general toxicity of the exhaust gas is negligible. Exposure to carbon monoxide results in the reduction of the available oxygen in the respired air. Symptoms are primarily due to oxygen deprivation, depending on the concentration of the carbon monoxide in the air and the duration of the exposure. The effect may be entirely negligible or, when severe, will manifest itself chiefly by injury to the nervous system, which characteristically shows the effect of oxygen deprivation to the tissues. Any effect on the circulatory system would be secondary and the result of a serious exposure to carbon monoxide, which would have resulted in a prolonged period of unconsciousness. Many observers, reporting in the past, attributed various changes noted in the blood vessels and heart to carbon monoxide exposures, but little evidence has ever been presented to justify these claims. The exposures assumed to have produced vascular effects were extreme. The vascular changes attributed to carbon monoxide exposure could not have occurred in the brief time mentioned, in which the appearance of a coronary occlusion was within a few minutes after exposure to the exhaust fumes.

POSTOPERATIVE PULMONARY EMBOLISM

To the Editor:—*Does general anesthesia contribute to fatal postoperative pulmonary embolism? This tragic complication continues to occur in spite of good operative and postoperative care, including such measures as maintenance of blood pressure during operation, elevation and massage of the lower limbs, elimination of pressure on the lower extremities, and early ambulation. Is the incidence of fatal postoperative pulmonary embolism greater after general anesthesia than after spinal anesthesia?*

F. A. Procunier, M.D.
Waterford, Ontario, Canada.

Answer.—This consultant does not believe that general anesthesia contributes in any way to nonfatal or fatal postoperative pulmonary embolism. With few exceptions, pulmonary embolism is a result of a bland thrombus in the vein, one which is not associated with phlebitis, and, therefore, the clot is not firmly attached and can become detached. This has been called phlebothrombosis in contradistinction to thrombophlebitis. Phlebothrombosis is probably due to two predisposing factors. One is an increased tendency of the blood to clot, resulting from tissue injury. It apparently does not make much difference whether the cause of the tissue injury is operative trauma, accidental trauma, or invasion of tissue by neoplastic disease or infection. Whenever there is tissue injury, there is an increased tendency of the blood to clot. The other predisposing factor is circulatory retardation, and it is for this reason that most phlebothromboses occur in the lower extremity, because of lack of movement of these extremities in a patient who is in bed. The incidence of pulmonary embolism apparently is no higher in patients operated on under general anesthesia than in those operated on under spinal anesthesia.

DIVERTICULITIS

To the Editor:—*An 82-year-old woman who had been in good health suddenly developed intestinal obstruction due to an inflammatory diverticulum in the sigmoid colon. A cecostomy was performed to relieve obstructive symptoms. The patient's condition returned to normal except for a profuse watery fecal discharge through the fistula, requiring four heavy dressings daily. At the time of writing, three months after onset, there has been no normal bowel movement. Should a colostomy be performed and the fistula closed?*

C. C. Dillon, M.D., Sidell, Ill.

Answer.—Since the patient's condition has returned essentially to normal, surgical exploration in the hope of resecting the segment of diverticulitis would be in order. If this cannot be done, a colostomy might be established in the descending colon and proximal to the diverticulitis. In due time, and possibly several months after resection or after colostomy, the cecostomy could be closed. This should make the patient much more comfortable.

PROTEINURIA

To the Editor:—*What is the significance of a finding of 2+ or more albumin in the urine with or without 5 to 10 red blood cells or 5 to 10 leukocytes? In review of hospital records, this has been a common finding in patients who are hospitalized for conditions other than genitourinary disease. Does this show a lowering of kidney reserve, or is it just a manifestation of a generalized toxic condition? A woman who is menstruating has 4+ albumin in the urine with gross blood. Can this finding be attributed entirely to menstruation? A patient who comes in for an operation, such as a herniorrhaphy or dental extraction, may show 2+ albumin with 10 red blood cells and 10 leukocytes in the urine. Is this significant of genitourinary pathology? A point of discussion is that these findings are to be ignored if they are not based on catheterized specimens.*

Nerico W. Pioppi, M.D., Southbridge, Mass.

Answer.—The finding of 2+ albumin in the urine in the presence of a generalized toxic condition is of no particular significance, but, in an otherwise healthy patient with only a few white or red blood cells in the urine, such a finding should be carefully investigated. In the menstruating woman, the finding of a high degree of albuminuria can be entirely normal. The best way to determine this is to wait until the menstrual period is over and recheck one or two more specimens. It is true that, with the highly sensitive tests so commonly used today, the presence of a trace or up to 1+ albuminuria may be within normal limits. This consultant does not believe that it is always necessary to have a catheterized specimen of urine to appreciate the importance of albuminuria, but it is impossible to make any suggestions concerning cellular findings in the urine specimen from a woman unless it is a catheterized specimen.

GASES IN NEON LIGHTS

To the Editor:—*What gases are used in neon lights? Are they injurious to persons working with them?*

W. J. Tucker, M.D., Ashland, Wis.

Answer.—The gases likely to appear in the neon type of light, but not all in any one style or form, are neon, krypton, argon, xenon, and helium. All of these gases are essentially harmless, acting only as simple asphyxiants. Any damage connected with the manufacture of these light tubes is more likely to be identifiable with the phosphors contained rather than the gases. Although all beryllium is believed to have disappeared from ordinary fluorescent lighting tubes, it may be suspected that some beryllium may be surreptitiously introduced into some of the neon type of tubes. If this is true, this practice is more likely to exist in small rather than large manufacturing plants.

RESTORATION OF DIVIDED VAS DEFERENS

To the Editor:—*A 30-year-old man stated that at the age of 27 he had a partial vasectomy, which apparently failed in that the sperm count remained high. One testis had previously been removed, apparently because of a severe injury. The second time the vasectomy was performed, an inguinal incision was made and, presumably, a segment of the vas deferens was removed. The patient said his physician told him the vas was removed "down next to the prostate." The patient has two children by a former marriage, and now he is anxious that his present wife become pregnant. The problem seems to resolve itself into two approaches: (1) reanastomosis of the divided vas deferens and (2) aspiration of spermatozoa from the epididymis. Please offer suggestions as to the details of aspirating spermatozoa for cervical injection and give references for surgical restoration of the divided vas deferens.* *M.D., Illinois.*

Answer.—Reanastomosis of the divided vas deferens has proved successful to a varying degree. In recent years several reports (O'Conor, *J. A. M. A.* 136:162-163 [Jan. 17] 1948; Dorsey, *J. Internat. Coll. Surgeons* 27:453, 1957) have been made of a series of such operations which have proved to be successful in many cases. If reanastomosis is attempted, it should be done by a urologist who has had wide experience with this operation. Aspiration of spermatozoa from the epididymis has not been successful in many cases. In the first place, it is difficult to collect a sufficient number of spermatozoa by aspiration to achieve insemination. Furthermore, the spermatozoa would not have opportunity to mature without having passed through the epididymis and vas. The possibility of collecting a sufficient number of spermatozoa by means of an operation causing dilatation of the vas has been suggested.

DISINFECTION OF FLOORS

To the Editor:—*What germicide is best suited for cleaning floors that might be contaminated with Mycobacterium tuberculosis? Is any antiseptic more effective than phenol?*

Denvil F. Crowe, M.D., Paris, Tenn.

Answer.—Washing the floors and woodwork of rooms contaminated by tubercle bacilli with soap and hot water and subsequent wetting with a 2 to 5% solution of *o*-phenyl and methyl phenols remains the standard recommendation. Among the newer compounds, a 2.5% solution of *o*-phenyl and *p*-*tert*-amyl phenols with potassium ricinoleate is highly recommended; it has the advantage of being odorless.

REPEATED CONGENITAL DEFECTS

To the Editor:—*One year ago, a 22-year-old woman delivered a female infant who died shortly after birth due to bilateral cystic kidneys, hydrocephalus, porencephalic cyst, intra-atrial septal defect, and tricuspid valve atresia. Recently, she delivered a second female infant who died shortly after birth due to bilateral cystic kidneys, hydrocephalus, and encephalocele. She has had no other pregnancies. Neither the husband nor the wife has any congenital defects, and there is no history of such defects in their families. What advice should be given to this couple regarding a future pregnancy? Should husband and wife be investigated for congenital kidney defects? Would semen examination be of any value?*

Edward B. O'Connell, M.D., New Haven, Conn.

Answer.—The abnormalities of these infants could be due to a combination of hereditary defects and "errors of development." It is impossible to determine which is the more important in each individual abnormality. Hydrocephalus is often inherited as a recessive characteristic. If it is inherited in this instance, both parents had the tendency, which was not, however, expressed in them. The statistical expectation would be that one child out of every four would be hydrocephalic. Since the mother has already borne two affected children, there would be a good chance that the next one would be free from this defect, but the other serious defects might be present. In view of the number and seriousness of these, the prognosis is so doubtful that the couple might well be advised not to risk another pregnancy. Semen examination would be of no value.

HYPOGLYCEMIA

To the Editor:—*Is there any truth to the theory that a low blood sugar level (cause unknown) may be made worse by the administration of dextrose or the frequent use of glucose (hard candy) given orally? The supposed theory is that the dextrose will activate the pancreas to produce more insulin and thus further reduce the blood sugar level. A patient had a blood sugar level of 52 mg. % and weak spells. Exploration was done, and no tumor could be found in his pancreas. He now says he gets along better if he uses no sugar and thinks his blood sugar level is up to 105 mg. %. Is this likely?*

George C. Christie, M.D., Canon City, Colo.

Answer.—As far as an immediate effect is concerned, the administration of dextrose tends to elevate the blood sugar level, but as a long-term effect in persons with so-called functional neurogenic hypoglycemia a high carbohydrate intake usually aggravates the condition. This comes about presumably because of an overly great response of insulin-producing cells to the stimulus of a rising blood sugar level. In such persons the blood sugar level after an overnight fast is normal but may fall to hypoglycemic levels two or three hours after eating. Treatment consists of (1) a diet low in carbohydrate, liberal in protein, and with enough fat to provide adequate calories; (2) between-meal snacks which are low in carbohydrate; (3) small doses of phenobarbital and belladonna; and (4) relief from tension and stressful situations. Assuming that the patient in question does not have an islet cell tumor, these measures may prove beneficial. The article by Conn and Seltzer (*Am. J. Med.* 19:460, 1955) should be consulted.

POSTERIOR PITUITARY INJECTION AND GENERAL ANESTHESIA

To the Editor:—*Is the use of posterior pituitary injection as a local vasoconstrictor in surgery contraindicated when general anesthesia is used?*

M.D., New York.

Answer.—In anesthesia produced by agents having a direct action on the heart and, under some conditions, all commonly used general anesthetic agents are cardiac depressants, posterior pituitary injection should be avoided as a vasoconstrictor. This is due to the fact that this drug contains vasopressin tannate, which has a constricting action on the coronary arteries, and, when this is combined with myocardial depression, pronounced hypotension may result. Myocardial and coronary artery disease must also be considered as contraindications to the use of this drug. If this agent is slowly absorbed, there is little likelihood of a severe reaction, but as long as there is a possibility of accidental intravascular injection one must be prepared to accept the results of coronary constriction. If the patient is predisposed to asthma or if cyclopropane is being used, laryngospasm, bronchospasm, or bronchorrhea may also result from posterior pituitary injection.

Reference

Parsloe, C. P.; Morris, L. E.; and Orth, O. S.: Relationship of Various Anesthetic Agents to Action of Pituitrin, Pitressin, and Pitocin, Anesthesiology **11**:76-93 (Jan.) 1950.

TESTICULAR TUMORS

To the Editor:—*Is there any evidence that testicular tumors occur with any greater frequency in men who have had vasectomies?*

Joe J. Horn, M.D., Plainview, Texas.

Answer.—Vasectomy has no effect on the testis other than obstruction to the passage of its spermatozoa. Spermatogenesis and formation of Leydig's cells continue undisturbed. A review of the literature has disclosed no increased incidence of tumor formation of the testis after vasectomy. Occasionally, spermatozoa are found invading the tissue of the epididymis, producing a tumor-like swelling which is actually granulamatous. Such granulomas are not necessarily associated with vasal or epididymal obstruction.

COUGHING AFTER CATARACT OPERATION

To the Editor:—*A 60-year-old man has cataracts of both eyes. The vision of the right eye is 0 and of the left 20/250. The patient also has hypoparathyroidism, which is controlled, and more important, bronchiectasis of both lower lobes which causes frequent coughing. Is it possible to stop coughing during and for a few days after the cataract operation? Is it possible to keep the intraocular pressure steady after the cataract operation? The tension of the eyes is normal.*

Arnold Ernest Aszody, M.D., Corona, N.Y.

Answer.—With the present-day technique of cataract extraction and with the use of corneoscleral suturing of the incision, a patient who coughs during or after such an operation is no longer considered with the fear that was formerly held. An evaluation of the bronchiectasis should be made prior to cataract extraction. After this, the management of the pulmonary condition should be undertaken to clear up any infection. Both before and after operation, small doses of codeine or similar drugs may be used to suppress but not abolish the cough. The intraocular pressure can be maintained postoperatively by an adequate iridectomy at the time of operation, the use of miotics locally, and the oral use of any of the effective, long-acting inhibitors of cholinesterase, such as acetazolamide, chlorothiazide, and ethoxzolamide. None of these drugs should be used without the proper indication, namely, increased intraocular pressure.

GAMMA GLOBULIN DEFICIENCY

To the Editor:—*Two small boys have an extreme gamma globulin deficiency. The father's employment requires long periods outside the United States. Since these children probably cannot develop active immunization, is there any value in giving them anti-diphtheria-pertussis-tetanus (DPT) injections and would it not be dangerous to vaccinate them against smallpox? Would these children not have as much protection with their regular gamma globulin injections as if they were receiving active immunizations?*

Spencer C. Manrodt, M.D., Melbourne, Fla.

Answer.—It would be hazardous indeed to vaccinate these boys against smallpox. The risk of giving them DPT injections would far outweigh the possible good obtained. For maximum protection it would be safer and preferable to administer intramuscularly or subcutaneously (not intravenously) the proper dosage of pooled adult gamma globulin once every four to six weeks. The dose is computed by body weight. Infectious hepatitis, measles, poliomyelitis, and possibly other diseases should be prevented or ameliorated by 5 to 10 ml. of potent gamma globulin per 100 lb. of body weight. The antibody content of 1 ml. of gamma globulin should be the equivalent of 25 ml. of whole serum. Its use is accompanied by less discomfort and no reactions or hazards, if syringe and needle are properly sterilized and the site of injection properly cleansed with 70% alcohol and a sterile pledget of gauze or cotton. Gamma globulin deficiency can be managed by the administration of 0.1 ml. per kilogram of body weight monthly.

SMOKE POISONING

To the Editor:—*Are there lethal factors beyond carbon monoxide, heat, and asphyxia inherent in the smoke poisoning encountered in a burning building?*

I. G. Frohman, M.D., Rockaway Beach, N. Y.

Answer.—Depending on the combustible content of the building, the possibilities are legion. Among others are nitrogen dioxide leading to pulmonary edema, irritant aldehydes conducive to pneumonitis, and hydrogen cyanide from the partial combustion of such objects as wool rugs or wool upholstery. Sulfur dioxide is always present and might reach lethal concentration. Partial combustion may lead to the presence of hydrogen sulfide. Carbon dioxide may be active over and above its simple asphyxiant properties. Depending on the nature of the fire-fighting equipment, phosgene may arise from the decomposition of carbon tetrachloride. Particulate matter, such as carbon, contributing to the smoke may enhance the activity of some of the chemicals mentioned. This list could be expanded extensively. Many of the larger fire insurance companies publish lists of the major constituents of poisonous smokes.

TORTICOLLIS

To the Editor:—*Is there any satisfactory treatment for chronic wryneck? In a 48-year-old woman who is going through the menopause and whose general health is reasonably good, this condition has come on in the past few years. She now holds her head constantly on the left and at times she pushes it back to the normal position with her left hand. She was told to take meprobamate and found it of some aid. The general examination is negative except for moderate scoliosis in the cervicothoracic spine.*

Alan R. Anderson, M.D., Freeport, N. Y.

Answer.—Spasmodic torticollis is one of the movement disorders for which there is no satisfactory treatment. Tranquilizers, such as meprobamate, occasionally give slight relief, and some of the anti-Parkinsonian remedies may be of slight benefit; however, for the most part, drugs have little effect. Neurosurgical intervention is occasionally recommended but may provide no real improvement. This has consisted in removing a portion of the hypertrophied sternocleidomastoid muscle and section of various of the upper cervical roots. More recently, destructive lesions of the basal ganglions have been tried. These patients sometimes are helped by psychiatric counseling when there is evidence of marked emotional instability.

"TRI-OPTIC LENS"

To the Editor:—*An article in* Newsweek Magazine *(Oct. 27, 1958) stated that there is a tri-optic plastic lens that will give good vision. Is such a lens available on the market? Where can it be purchased?*

Odell J. Kirksey, M.D., Mulberry, Ark.

Answer.—Experience at several centers has shown that, generally, near-blind persons find more useful a particular lens for whatever their specific visual requirement may be than the complicated lens described. A high-power, relatively inexpensive lens fitted in a spectacle frame can be used for reading. The best correction can be used for ordinary travel. These two corrections can be combined in a bifocal lens, if such is desired. If a nearly blind person wishes to see something like a street sign, he can use a pocket telescope such as the "penscope," available through the American

Foundation for the Blind, 15 W. 16th St., New York 11. For sports events, some patients like to use low-power binoculars. Before any special lenses are fitted, a person should have a thorough ophthalmological examination. Apparently the "tri-optic lens" is available only through its inventor.

CAUSE OF OLD INFARCT

To the Editor:—*A man, aged 29, has an old healed infarct of the anterior coronary branch without any significant history other than that he was temporarily paralyzed at the age of 9 by a bolt of lightning. Clinically, he is quite well. Could this accident have damaged the vessel?*

Malcolm L. Raymond, M.D., Johnstown, Pa.

Answer.—A generalized electric shock should not have a selective effect on a coronary branch. At the age of 9 years, atherosclerotic damage is not likely. It is possible to have a relatively painless infarction of a coronary branch. The patient's pain threshold would be a factor.

TREATMENT OF HEPATITIS

To the Editor:—*In a recent issue of a German medical publication,* Drug Research, *an article appeared on the treatment of different forms of hepatitis by means of a substrate consisting of supravital liver cells coupled to a bacterial haptene. Please comment on this type of therapy.*

Emily A. Svoboda, M.D., Chicago.

Answer.—The variable and unpredictable course of any given case of hepatitis has led to claims for many forms of therapy which further experience has shown to have been unfounded. The use of "supravital liver cells coupled to a bacterial haptene" has no rational basis, nor is there any convincing evidence of its efficacy. For the present, reliance on generally accepted symptomatic and supportive measures for the treatment of hepatitis is indicated.

NUTRITION FOR A PATIENT WITH TWENTY CENTIMETERS OF JEJUNUM

To the Editor.—*An additional therapeutic measure to those that were offered in the Questions and Answers column on the subject of nutrition for a patient with 20 cm. of jejunum* (J. A. M. A. 169:*201 [Jan. 10] 1959) is the use of corticosteroids. We have given prednisone (and before that cortisone) with much success to patients with jejunoileitis who have undergone massive resection. The usefulness of corticosteroids lies in their ability to increase the absorption of fluids, electrolytes, and nutrients from the intestines. The dose may vary from 15 to 30 mg. of prednisone per day. This should be fortified at monthly intervals by ACTH and, in this case, by a male hormone. Despite the colostomy, the administration of steroids should be rewarding. The use of the term regional ileitis for such extensive disease requires some elaboration. Ileocolitis, regional enteritis, and nonspecific jejunoileitis are more precise terms.*

A. I. Friedman, M.D.
405 State St.
Hackensack, N. J.

SMALLPOX VACCINATION

To the Editor:—*An item in Questions and Answers (J. A. M. A.* 169:*198 [Jan. 10] 1959) stated that failures to develop a primary take of smallpox vaccination were due to faulty vaccination technique or to the use of vaccines which had lost their potency because of improper or prolonged storage. A woman has had repeated vaccinations for smallpox without a take. Vaccinations have been performed by a number of physicians, including myself, with vaccines that had proved effective in other patients. A son, aged 2½ years, also has had repeated vaccinations without a take. A daughter, aged 10 months, has had a successful take. I am wondering if others have had similar experiences and if other factors in the take of smallpox vaccination are to be considered.*

Horace A. Deford, M.D.
34th Air Division (Defense)
Kirtland Air Force Base, N. Mex.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Experimentally it has been shown that the state of nutrition and hormone balance of an animal affects the growth of vaccine virus and the lesions it induces (Smadel, in Viral and Rickettsial Diseases of Man, edited by Thomas E. Rivers, Philadelphia, J. B. Lippincott Company, 1952). In man it may be that due to these or other factors some persons are truly resistant—at least temporarily—to smallpox vaccine. There is, however, evidence that such persons are rare and, for the most part, repeated failures to take are due to a faulty technique or to the use of an inactivated vaccine. The fact that a particular lot has proved successful in other patients does not necessarily mean that it should also be successful in a particular individual. As stated by Leake (Questions and Answers on Smallpox and Vaccination, Public Health Report, reprint 1137), "differences in skin receptivity may occur independently of the condition of the individual as regards true immunity. . . . Some individuals may be resistant . . . to a lot of vaccine which gives success generally in other individuals, but are not immuned against smallpox when exposed, nor against vaccination when a fully potent lot of vaccine is used."*

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EFFECTIVE SYSTEM OF BACTERICIDAL CONDITIONING FOR HOSPITALS

Perry B. Hudson, M.D., Grant Sanger, M.D.
and
Edith E. Sproul, M.D., New York

Control of the hospital environment is an important initial step in the campaign to control hospital infections. Daily treatment of the patient's entire environment with chemicals is not feasible, but bactericidal treatment of the air can and must be continuous. Four materials are here described for use as waxes, in floor preparations, and on air filters; for application as wax to metal and glass; for spraying walls, ceilings, floors, and mattresses; and for laundry, furniture, and draperies. Their effectiveness was studied in a comparative experiment in which alternate wards in a hospital were studied bacteriologically, the air being recirculated at various set rates. It was found possible to bring about a steady reduction of the bacteria in the air without depending on a central air conditioning system. A major portion of the bacteriological killing depends on procedures other than air filtration. The methods suggested were found consistent with ordinary hospital housekeeping techniques.

An increase in mortality and morbidity from infections in hospitals is attributed to dissemination of bacteria which are resistant to antibiotic drugs. Most prominent among the resistant strains of bacteria is the coagulase-positive Staphylococcus aureus (80/81 strain). The serious nature and wide currency of the staphylococcic infection problem has been emphasized at large conferences held specifically for discussion of this topic. The problem is now of sufficient magnitude to demand the establishment of infection committees in all institutions within which sick persons are housed.

The committee on infections in the Francis Delafield Hospital made a decision to undertake control of the hospital environment as an initial step in its campaign to control hospital infections. For this purpose it has been necessary, first, to define precisely the elements comprising the hospital environment; second, to find the proper agents to be used in the control of the environment; third, to conduct controlled experiments utilizing the agents and methods selected; and, fourth, to evaluate objectively the altered environment.

Hospital Environment

The hospital environment is defined in a personal rather than a geographical way. The person in relation to whom this definition is made is the patient. His environment is made up of a multiplicity of contributions from all of the persons, things, and mediums with which he has contact.

From the departments of urology, pathology, and surgery, Francis Delafield Hospital, Columbia-Presbyterian Medical Center.

The air in which the patient moves and which he breathes is a principal element of the environment. The persons and things which both the patient and the hospital air touch contribute to the total constitution of the environment.

The relative importance of any portion of the environment depends on the intimacy, frequency, and duration of contact which the patient may have with that particular unit. The air and linen supply for patients probably exceeds in relative importance the bacterial flora on a ceiling. On the other hand, even bacteria on a ceiling assume importance when and if they enter the ocean of air to which both the patient and his linens are exposed. Food as well as its preparation was deliberately omitted from this experiment.

Formulations Used in Removal of Bacterial Contamination in Hospital

Formulation A (for waxes, floor preparations, and air filters)	%
Silver nitrate	1.32
Ammonium thiocyanate	1.32
Triton X45	5.04
Hycryl A-1000	26.01
Poloco 380	33.61
Nuodex 100	0.35
Propylene glycol	0.32
Water	32.03
Formulation B (for metal and glass wax)	
Dialkyl*dimethyl ammonium chloride	0.0214
o-Hydroxybenzoic acid	0.0140
Bis(n-tributyl) tin oxide	0.0151
2,3,5-Triphenyl-2,1,3,4-tetrazolium chloride	0.0015
2-Amino-2-hydroxymethyl-1,3-propanediol	0.0168
2-Hydroxyethyl tetramethyl ammonium chloride carbamate of zinc chloride	0.0105
Dimethylcarbinol	0.0216
Neutroleum gamma	0.0008
Inert ingredients	99.8982
Formulation C (spray for walls, ceilings, floors, mattresses, and laundry)	
Dialkyl*dimethyl ammonium chloride	0.0214
Salicylic acid	0.0140
Bis(n-tributyl) tin oxide	0.0151
Inert ingredients	99.9495
Formulation D (spray for laundry, furniture, and draperies)	
Salicylic acid	0.0301
Arquad 2C-75	0.2064
Neutroleum gamma	0.0273
Bis(n-tributyl) tin oxide	0.0325
Isopropanol 99%	0.0957
Spice bouquet	0.0082
Inert ingredients	99.5998

* Alkyl groups as in the fatty acids of cocoanut oil.

The bacterial populations in the respiratory system and on the skin of patients, hospital staff, and visitors are considered to be an uncontrollable portion of any patient's environment. They are also unpredictable. Therefore, removal of bacterial contamination, not simply detection of human carriers per se, is one of the prime objectives in the design of an environmental control system. This concept is important in our program for bactericidal conditioning of hospitals. The hospital has been changed from a repository for germs into a self-decontaminating area. These alterations in environment have been achieved by the addition of bactericidal substances and by removal of bacteria.

Agents and Methods

The difficulty in selecting bacterial substances was one of finding drugs of lasting germ-killing properties. Daily treatment of the patient's entire environment with chemicals is not feasible. It is also acknowledged that the bactericidal treatment of air must be continuous.

The low-cost, long-lasting bactericidal properties, ease of applicability, wide-range spectrum response, and low toxicity of the agents finally selected were decisive factors. A list of these formulations is contained in the table. Bactericidal conditioning was designed for both efficacy and duplicability in other hospitals.

At the laundry, hospital linens were treated by addition of bactericide to the rinse water for sheets, towels, blankets, pajamas, curtains, and staff uniforms. The concentration selected was such that substantivity would be maintained only until the next washing cycle. A more permanent effect (for example, for the life of blankets) can be obtained by using materials impregnated with the bactericide at manufacturing levels. However, in order to achieve the variable control essential for this experiment, the laundry technique was used.

Ceilings and walls of each ward, ward corridor, utility room, lavatory, and solarium in the patient areas were washed and then sprayed with a bactericide. Waxes for glass, furniture, and metal were prepared with added bactericide. Every article within patient contact was either washed or sprayed with one of the bactericidal formulations. Mattresses and pillows were sprayed and then covered with bactericidal plastic covers. All covered areas such as radiator shields and ducts were opened, cleaned, and sprayed. The floor wax contained bactericide preparations. Routine floor care followed, with bactericide added to the mop water.

The hospital air was controlled as follows: Patient areas were under positive pressure, and areas of known, continual infection were subjected to negative pressure with external exhaust. Exhaust fans were also placed at one end of the ward corridors. Fresh air intake window fans were placed in each ward. Air recirculation was maintained in the wards, corridors, and solariums by means of small recirculation units for bactericidal filtration. Window input and recirculation units contained double filters impregnated with bactericide. The total volume of air was recirculated once every 10 minutes (that is, recirculation time equals 10 minutes, or RT=10). This recirculation time (RT) was varied as the experiment progressed. Filters were changed on a cosmetic rather than germicidal basis, since the former preceded the latter need by some weeks. After the initial stage of preparing test areas, bactericide was used only in mop water, water used to wipe off furniture, and aerosol spray bombs for spot disinfection purposes.

Hospital Experiment

The Francis Delafield Hospital is a 300-bed general cancer hospital staffed by Columbia University and administered by the city of New York. Its general plan is indicated in figure 1. The hospital contains no central air conditioning plan or equipment.

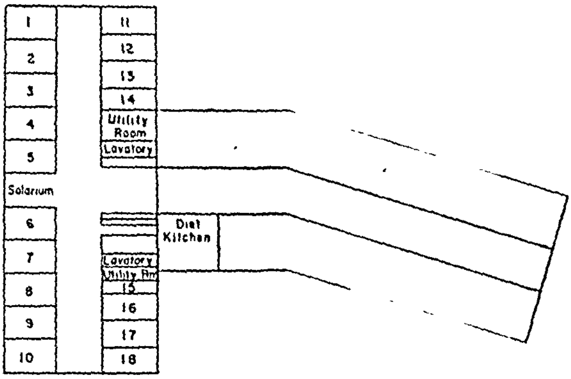

Fig. 1.—General plan of Francis Delafield Hospital. Second, third, fourth, and fifth floors have 40 six-bed wards, 10 to each floor (areas 1 to 10 in diagram), which constituted the test and control areas studied. Areas 11 to 18 are two-bed or three-bed rooms.

General Bacteriological Evaluation of Hospital Environment.—For three days, consecutive culturing was done in all patient and service areas, by streak, poured plate, and open dish methods, which included fomites as well as air. Culture tubes and plates were marked by number. Colonies were counted and identified by the hospital bacteriological staff, who did not know the origin of the cultures. Results were entered by code in log books, the key to which was held by one member of the committee on infections. A number of potential sources of infection were discovered, but no changes were made in the hospital routine throughout the course of all the experiments.

Air samples were collected on opened, preincubated Petri dishes containing sterile nutrient agar. Exposure time was one hour. Cultures were made during times of day when average patient and visitor activity was in progress. Cultures were incubated at 37 C for 20 hours. Bacterial colonies were counted with the Quebec dark-field counter and a four-power lens.

Colonies resembling Staph. aureus were reincubated at room temperature for two days and reexamined for pigment production. For all cultures the bacteria were identified by colony characteristics and by microscopic examination of Gram-stain smears from individual colonies.

Staphylococcus colonies were replated on sheep blood agar medium, and the presence of hemolysis after incubation was recorded. Coagulase tests were also performed on these strains. The penicillin impregnated disk method with 18-hour culturing on agar plates was used to determine antibiotic sensitivity or resistance. (Detailed studies on organisms other than staphylococci will be published elsewhere.)

Preliminary Control Experiment.—The statistical consultants for the hospital experiment requested that it be conducted on the basis of alternating wards as controls and as bactericidally conditioned areas on each of the four inpatient floors (fig. 2). After this recommendation, alternate wards were treated by the methods previously described. For control wards, only routine hospital procedures were used, except that the same type of window input and air recirculation fans were installed to keep air procedures similar. Air control for this experiment consisted of filtration of the locally recirculated room air once every 10 minutes (RT=10).

In order to use the alternate ward system, it is necessary to maintain closed doors between the bactericidally conditioned wards and the alternating control wards. Both ambulatory patients and hospital staff personnel have easy access to these doors in our hospital. Closure of the doors for many weeks would be required for evaluation of altered population of bacteria in the air of the conditioned areas.

The committee on infections was unable to secure the level of cooperation needed for full evaluation of this checkerboard technique. Nevertheless, alternate ward conditioning did result in an average 50% decrease of colony counts in air of conditioned wards. Experience with this alternate ward experiment has reemphasized the need for bactericidal conditioning, agents, and methods which are consistent with routine hospital housekeeping measures and which require little or no change in habits or therapeutic techniques.

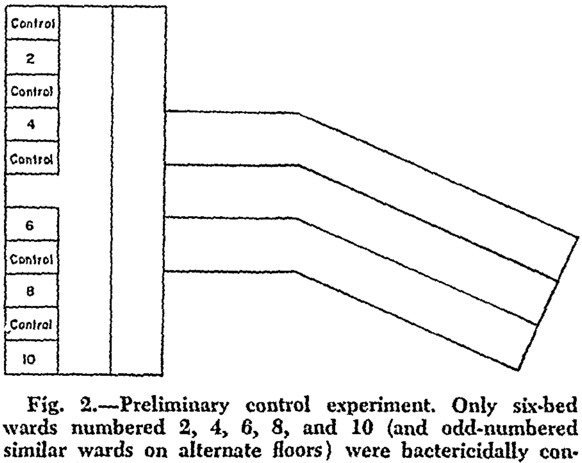

Fig. 2.—Preliminary control experiment. Only six-bed wards numbered 2, 4, 6, 8, and 10 (and odd-numbered similar wards on alternate floors) were bactericidally conditioned. Doors permit not only control ward air but also contaminated corridor air to enter each conditioned ward whenever door is opened.

Long-term Forty-Ward Hospital Experiment.—After the preliminary experiment, two patient floors were completely exposed to bactericidal conditioning. Wards, solariums, utility rooms, lavatories, and diet kitchens were washed and sprayed, and air control measures were instituted in these areas as well as in ward corridors.

As the experiment proceeded, changes were made in the air control measures. Principally this consisted in working out better exhaust techniques to control negative pressure areas with more efficiency and less noise, while recirculation times within the patient wards were raised and lowered to find the exact point of bactericidal control in the presence of the most extreme conditions of contamination. Simultaneously, this afforded an opportunity to ascribe relative importance to air control measures and the other means of bactericidal conditioning.

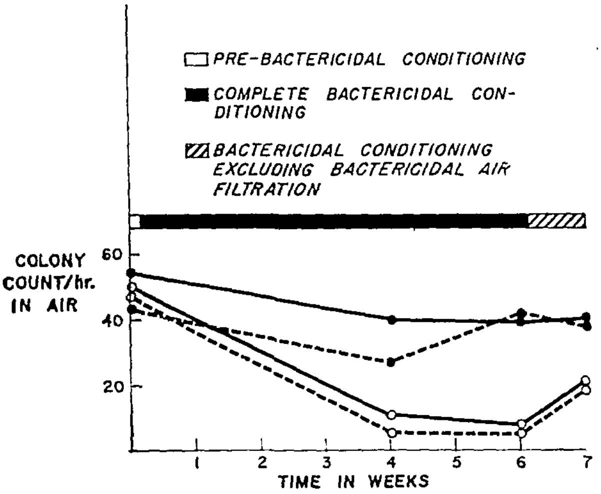

Fig. 3.—Effect of bactericidal action on hospital environment. Each point on graph is average value of 60 air cultures. Duplicate cultures in all 10 of six-bed wards on all four floors were made for three consecutive days; thus, 60-culture average of each floor has been made. Lines with black circles represent control floors; with open circles, test floors.

After complete conditioning of the two floors, they were designated as test floors; the remaining two patient floors were used as controls. It was recognized that the previous checkerboard treatment applied to the control floors would tend to lower their total bacterial counts and apparently lower the system's efficacy. This was accepted as a condition of the experimental control.

Air cultures were made on each floor daily, with two cultures to each ward room. Culturing was done in corridors, solariums, isolation rooms, and nurses' stations. At intervals, surface and fomite cultures were also taken.

All Petri dishes were identically placed during the experiment, one near and to the right of the corridor door, the other to the left and near the far window. Exposure time was one hour at varying intervals ranging from maximum visitor exposure to late night quiet. Culturing for final evaluations was done during evening visiting hours.

Results

Long-term Forty-Ward Experiment.—The effect of long-lasting bactericidal action on the hospital environment as interpreted through air cultures is shown in figure 3. The initial values (in colony counts) on the control floors were 54 and 43; those on the test floors, 47 and 50. Four weeks later, the control floors had values of 27 and 40; the two bactericidally conditioned floors yielded air counts of 5 and 11 respectively. One and one-half months after bactericidal conditioning, the control floors were found to have counts of 39 and 43, while the test floor counts were 5 and 8, a reduction of 87 and 82% respectively.

It next seemed desirable to ascertain the relative value of the main components of the system used to accomplish this result. The last point on each of the four graphs in figure 3 represents the average cultures one week after the bactericidal agents were deleted from the air filtration process. The remaining decrease in bacterial colony counts on the test floors (to 18 and 20 respectively) below the control values (38 and 40 respectively) is attributable to components of the bactericidal conditioning process other than those directly applied to air.

Approximately two-thirds of the bactericidal effectiveness in this experiment may be attributed to elements of bactericidal conditioning not related to bactericidal filtration of air. Under conditions of extreme contamination of air, the relative value of bactericidal filtration increases somewhat.

Laboratory Model for Comparing Effectiveness of Bactericidal Conditioning Systems.—Early in our studies of hospital environmental problems related to pathogenic bacteria, the need for a model designed to approximate physical conditions encountered in a hospital building was apparent. It is useful in rapid screening for bactericidal efficacy of a large number of substances. Models also permit study of various methods of use for the selected bactericidal agents.

Our hospital model is similar to a bacteriological transfer chamber. It has six sides, is hermetically sealed, and contains 27 cu. ft. of space. This chamber is equipped with walls which are easily sterilized and which can be coated with various types of bactericides. It is furnished with an air recirculation machine which can optionally be equipped with different types of filtration devices.

The experiments in the model system have included the 80/81 strain of coagulase-positive, penicillin-resistant Staph. aureus. The details of four such experiments with this micro-organism are as follows: The principal point of reference quantifying the efficacy of agents and techniques is the rate of disappearance, over a period of two hours, of known numbers of specific micro-organisms grown in pure culture. The recirculation rate for all the experiments described here is one volume of air every four minutes (RT=4).

For experiments A, B, C, and D, two billion staphylococcus organisms were nebulized into the model hospital chamber in a single injection at the time recorded "0" for not more than two minutes' time. Experiment A consisted of simple recirculation without bactericidal coating of the walls and without bactericidal filtration of the air of any sort (control experiment). Experiment B consisted of filtration of the recirculated air through a synthetic fiber filter not containing bactericide; walls of the chamber were not coated with bactericide. Experiment C consisted of bactericidal filtration of the recirculated air; walls of chamber were not treated with bactericide. Experiment D consisted of bactericidal filtration of recirculated air; walls of chamber were coated with bactericide (see table).

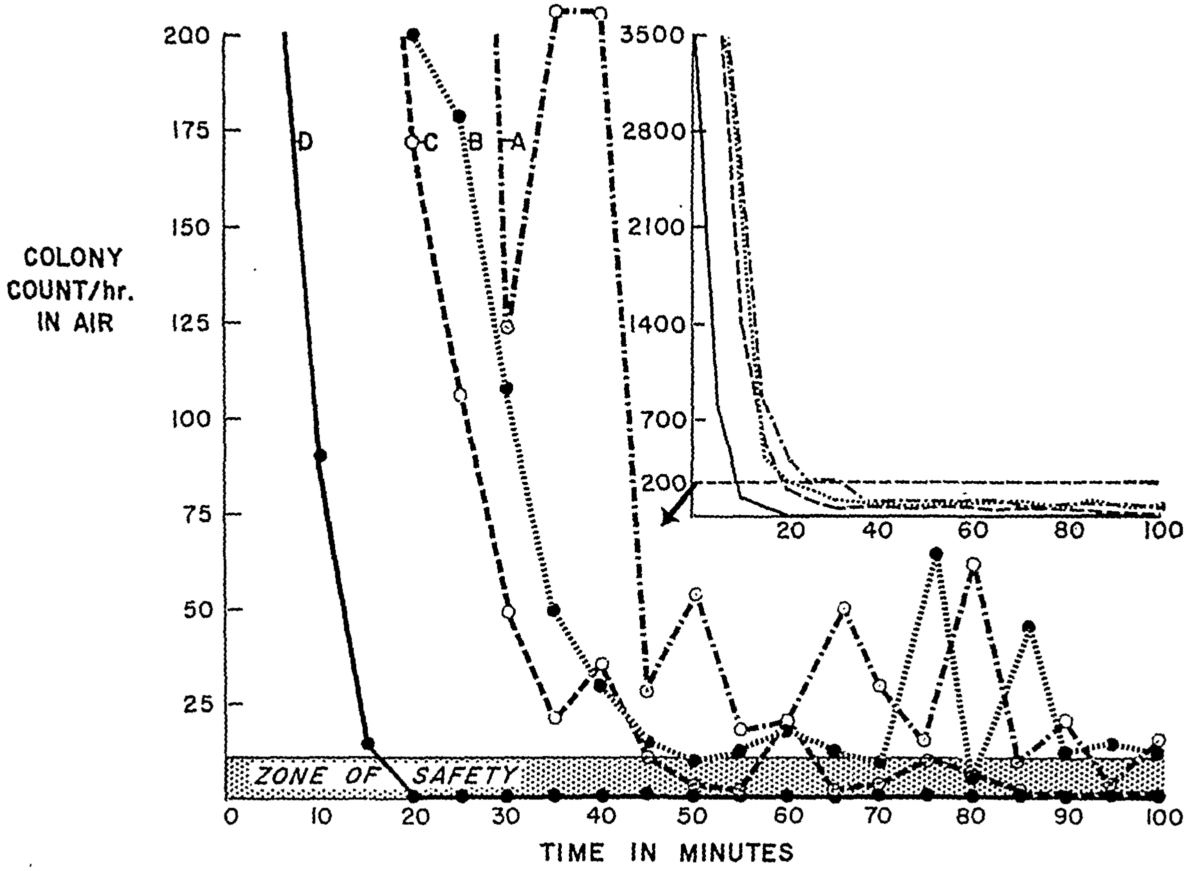

Fig. 4.—Colony counts in control and three experimental situations established in model chamber. Graph *A* is control; *B* represents serial counts when ordinary commercial filter is used; *C* shows effect of bactericidal filter without any other part of system; and *D* is model of hospital system found most effective—a combination of bactericidal filtration of air and bactericidal treatment of all surfaces.

Petri dishes used for air cultures in experiments A, B, C, and D were exposed for periods of five minutes each to cover, in duplicate, the entire period of two hours during which experiments in this model were run. The model chamber is equipped with built-in gloves long enough to permit remote, sterile handling of culture dishes throughout the experiments. The cultures could in this way be opened for specific five-minute intervals throughout the total time of the experiment so that cultures were done for consecutive five-minute periods.

The results of experiments A, B, C, and D are shown graphically in figure 4. For our model, as was the case with the hospital building, an upper limit of 10 colony counts for relative bacteriological safety was adopted. For the model system, the five-minute exposure periods are equated in the time-space scale to equal one hour. Therefore, the time required for reduction of the viable recirculated Staph. aureus suspended in air in these four experiments is the main criterion on which comparison of the different bactericidal techniques is based.

In experiment A (control), viable Staph. aureus organisms were erratically collected at dangerous levels of concentration throughout the entire experiment.

Similarly, in experiment B, viable organisms were collected, in somewhat lesser numbers, at dangerous levels throughout the course of the experiment despite use of an ordinary air filter.

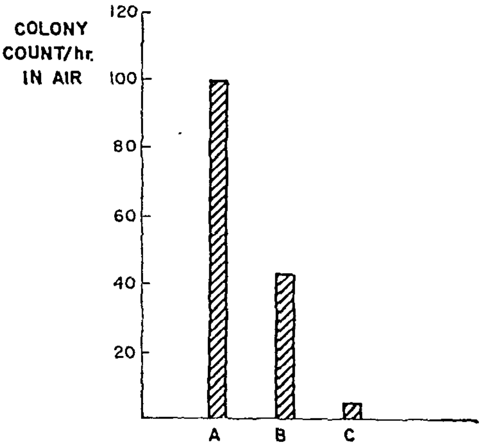

Fig. 5.—Colony counts. *A,* changing of ordinary, laundered blanket in ordinary hospital room yields level of 100 colony counts per hour. *B,* level of 43 results when bactericide-treated blanket is changed. *C,* only 5 colonies per hour are deposited when both room and blanket are bactericidally conditioned.

The bactericidally conditioned air filter used in experiment C produced a bacteriologically "safe" atmosphere in 45 minutes' time. At 65 minutes, a secondary rise to a level of 20 counts resulted. After 65 minutes, there is no return to levels above 10 counts. The zero mark was first reached in the 80-85 minute sample.

Experiment D was a model of the system finally adopted for our hospital bactericidal conditioning program. After the 15-minute sample, all of the culture plates failed to grow Staph. aureus.

This striking result gives objective support to the decision which resulted in the selection of agents applied in the fashion represented in experiment D for use in the actual hospital situation.

Corollary Hospital Experiments.—Our studies of the effectiveness of the bactericidal conditioning system included determination of the contributions from both persons and things to the population of pathogenic bacteria in the hospital air.

Hospital Blankets: A three-stage experiment on hospital blankets was performed. During the culturing period of one hour, no activity in the room was permitted. At the midway point in time, the blanket was stripped from the bed, turned over, and tucked around the mattress with the head and foot reversed. The blankets in each experiment were taken from the hospital linen supply immediately on return from the laundry. Activity was again forbidden for the remainder of the culturing period.

As shown in figure 5, when this procedure was followed in a two-bed ward room with a laundered blanket without bactericidal conditioning of the air, blanket, or room surfaces, a culture colony count of 100 was obtained. When this experiment was repeated in a room having no bactericidal treatment of either fomite surfaces or air, with a blanket bactericidally treated in the laundry, the colony count was 43. The third stage involved a bactericidally conditioned blanket and a room which had been given the same conditioning of air and surfaces as carried out in the hospital during the main experiment. The colony count then was 5.

Patients with Staphylococcic Infections: Figure 6 illustrates an experiment in two two-bed wards. Before bactericidal conditioning the air in each of these wards averaged 42 colony counts. After bactericidal conditioning they remained near zero for three weeks. Two patients, one with a mouth lesion and one with furunculosis of the shoulder (both of bacteriologically proved Staph. aureus origin), were admitted to room A. The recirculation factor was RT=10. After two days of high counts in room A, the patients were shifted to room B. Within six hours, room A, despite a high degree of personnel activity, was decontaminated to zero. In two days the air colony count in room B rose to 113.

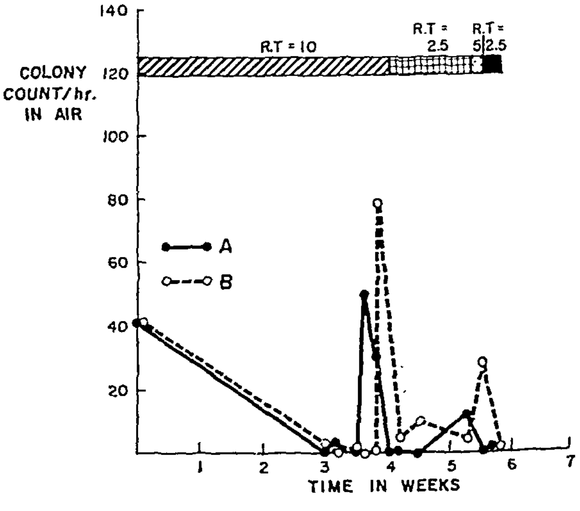

Fig. 6.—Effect on colony counts when patients with staphylococcic infections moved from room A to room B near end of fourth week. Note rapid fall-off of counts in room B when recirculation time (RT) decreased from 10 to 2.5 minutes.

At this point recirculation time was changed to RT=2.5. The air colony count dropped to 5 within six hours.

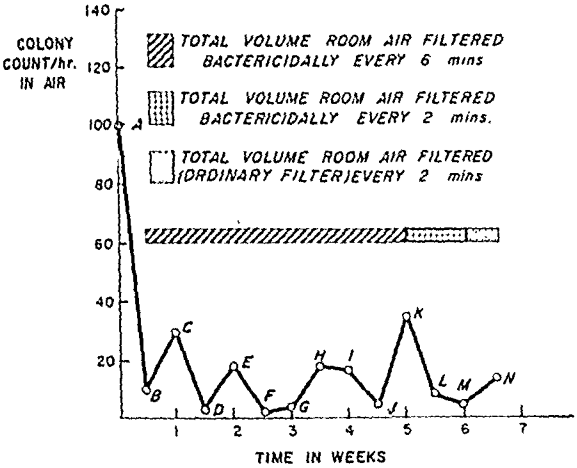

Fig. 7.—Continuous study of cultures. *A*, prebactericidal conditioning; *B*, bactericidal conditioning (checkerboard); *C*, door open to contaminated corridor; *D*, all wards bactericidally conditioned; *E*, door open to contaminated corridor; *F*, corridors bactericidally conditioned; *G*, door open to bactericidally conditioned corridor; *H*, four resident physicians examining patients; *I*, enema administered; *J*, normal ward activity; *K*, tracheostomy patient admitted to ward; *L*, normal ward activity; *M*, normal ward activity; and *N*, reversal experiment (bactericidal air filtration discontinued).

During the fifth week of this experiment, single bactericidal filters were substituted for double filters. The rise in air colony counts for both rooms prompted a return to use of double bactericidal air filtration. Colony counts immediately decreased again. In the middle of the sixth week, the recirculation time in room B was changed to RT=5. The count immediately rose to 28. The next day it was changed back to RT=2.5, and the count dropped to 2. Room A in the meantime remained at zero, except for the period when single filtration was attempted.

Continuous Gross Air Contamination: Study of the cultures taken during the course of many experiments indicates that the highest level of contamination contributed by patients is from male tracheostomy patients. Gross contamination from such patients has been demonstrated at a distance of 14 ft. from the patient. As shown in figure 7, the air recirculation utilized was RT=6 up to point K, when a male tracheostomy patient was admitted to the ward. The colony count then rose to 35. The RT factor was changed to 2, with a decrease in the count to 7 and then 4, in one week's time (points L and M). The rise at point N was due to the cessation of bactericidal air filtration during the "reversal" phase of the experiment.

During a three-week period a study was made of a six-bed ward to which patients were admitted with colostomies (2), an infected neoplasm of the lung, a rectovaginal fistula, a urinary tract infection, and a salpingo-oophorectomy. The problem of odor as well as air contamination was considered to be important. Details of this study are seen in figure 8.

Comment

The air control system finally adopted is shown in figure 9. It will be noted that the corridors are bactericidally conditioned and are included in the air control plan. Throughout our experiments of the last several months, it has been shown repeatedly that it is necessary to have an air lock adjacent to the patient areas in which the lowest possible contamination is sought. This measure prevents chance contamination of the air in the wards when doors are opened.

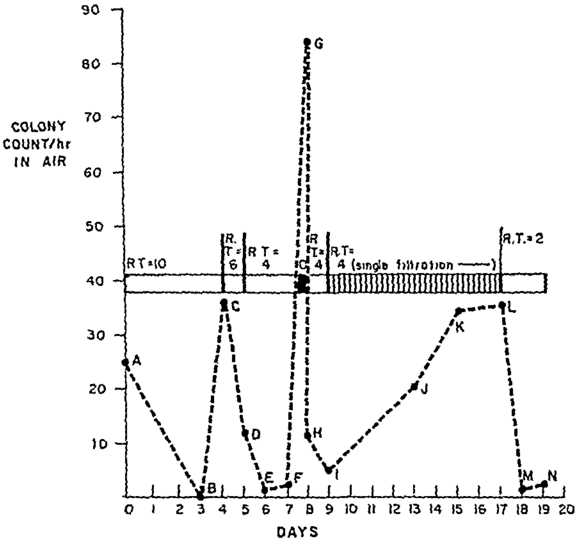

Fig. 8.—Study of odor problem. *A*, only patients with salpingo-oophorectomy and urinary tract infection in ward; *B*, bactericidal conditioning of ward; *C*, two colostomy patients and one lung cancer patient admitted to ward; *D* and *E*, recirculation of air changed to 6 and 4 minutes respectively; *F*, no change in conditions; *G*, bactericidal air filtration completely discontinued; *H*, 3 hours of reinstitution of air recirculation at RT=4; *I*, continuing low level of 5 counts; *J*, patient with rectovaginal fistula admitted; *K*, continuing rise in air colony counts during period of single-filter bactericidal filtration of air; *L*, high point before institution of double filtration of air with bactericidal filters and recirculation every 2 minutes; and *M* and *N*, levels maintained by double filtration at RT=2 even though no contaminating elements from patients have been altered.

It is readily acknowledged that great emphasis has been placed on the role which hospital air plays in making the environment either safe or dangerous. As Blowers and associates[1] have demonstrated, there is a direct correlation between surgical infection rates and air contamination. In addition, they have shown that the Staph. aureus carrier rate among both hospital patients and staff members decreases with a decrease in the degree of air contamination.

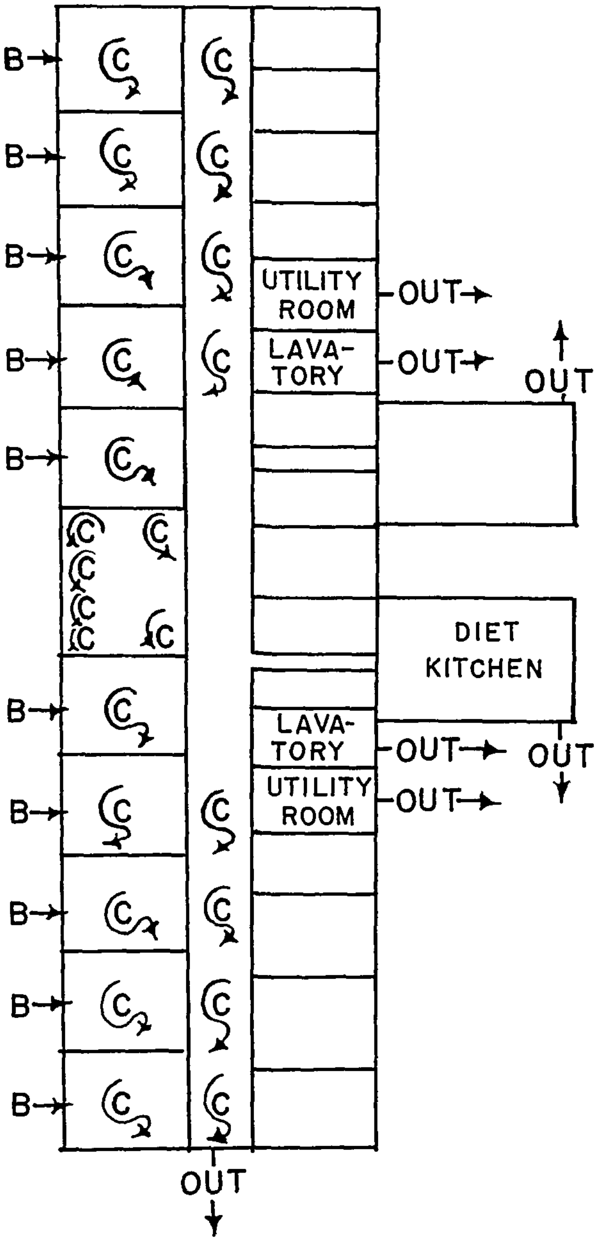

Fig. 9.—Air control system finally adopted. *B* indicates air intake window unit containing double bactericidal filter. *C* indicates interior recirculating fans with double bactericidal filters. All points labeled "out" are external exhaust fans.

On the other hand, the importance of inanimate objects in harboring bacteria has been elucidated by Walters.[2] His statement that "blankets are reservoirs and spreaders of bacteria in many hospitals" has prompted the blanket experiment included in the body of this report.

Our purpose has been to develop a system which utilizes commercially available substances and requires equipment useful in existing hospital buildings which are not centrally air-conditioned. The agents which we have used have been low in cost and have been used successfully. "Success" has been defined in terms of decontamination of the hospital environment as it is defined here in such a way that the basic conditioning process will probably not have to be repeated more than four times annually. That the hospital air must be continuously treated is an obvious fact. However, the removal of excessive contamination by means of variable control of the air recirculation rates through double bactericidal filters provides a flexibility in the sytem which it would otherwise lack.

The effect on the hospital environment through the use of the bactericidal formulations selected for the Francis Delafield Hospital experiments has been obtained because of the long-lasting bactericidal properties of the formulations used.

Summary

The current problem of hospital-acquired bacterial infections is believed to be a function of contamination in the patient's environment. Long-lasting bactericidal agents have been tested and found practicable and safe in hospital use. Hospital and laboratory experiments with these agents have been successfully conducted. More than four-fifths of the bacteria in air can be removed by the use of a combined air-and-fomite system of bactericidal conditioning. The agents and techniques for bactericidal conditioning are commercially available and reasonable in cost. Bactericidal control in hospitals is not dependent on a central air conditioning system. Bactericidal filtration of air without inclusion of other measures is not sufficient for an optimal result. Bactericidal conditioning is consistent with ordinary hospital housekeeping techniques.

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All of the bactericidal agents used in the hospital and laboratory experiments were formulated and supplied by the Permachem Corporation, New York.

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CONTROL OF INFECTIONS WITHIN HOSPITALS

SPECIAL REFERENCE TO PREVENTION WITHIN OPERATING ROOMS

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A searching study of hospital infections showed that blankets, shoes, the bottoms of trousers, straw brooms, dry mops, and certain types of vacuum cleaners were important spreaders of infection. It was found that the surgical area could be cleaned up and would remain clean until contamination was introduced. Personnel could learn so to conduct themselves with respect to masks, clothing, and shoes that they would not introduce contamination. An interchange zone was developed to separate the surgical area from uncontrolled areas, and a sexless, sizeless, reversible gown and improved footwear were adopted to facilitate changing when personnel are obliged to pass from one area to another. A fitted filter autoclavable mask was devised to prevent contamination of clean room air by respiratory exhalations of personnel or patients. If deep-seated wound infections with resultant systemic manifestations are to be prevented, the ultimate in asepsis must be attained, and no leniency can be tolerated.

Three years ago a study was launched into causes for infections occurring within Huggins Hospital and methods for prevention. This work has continued actively to date. Two years ago it was realized that nearly any patient who had entered the hospital clean during the preceding year and who had contracted an infection while there was the victim of an error in technique.[1] These errors include prophylactic use of antibiotics and steroid hormones used nonspecifically, but infection incidence in this hospital is influenced by these two factors only as they may have been induced by self, druggist, or practitioner administration to patients before they were hospitalized.

The most fundamental fact regarding the broad problem of infections occurring within hospitals is that clean or healthy tissues become infected because they are exposed to infectious agents at a level of virulence, concentration, or frequency of exposure beyond their resistive powers. Here in this fact, experience indicates, lies a practical approach to control measures. If reduced to axiomatic form, the fact would read: Where there is no contamination of healthy tissues, there is no infection. Restated in procedural terms, it would read: When necessary standards of sanitation and care are practiced in the protection of tissues from contact with infectious organisms, almost no infection will occur. The problem is one of cleanliness—how to attain it, and how to maintain it.

This article is a report of investigations made into the causes of infections in Huggins Hospital and a description of a control program which has now been proved to be medically effective, practical, and economically feasible. The studies were made primarily because of seven wound infections that occurred in the course of 356 operative procedures after establishment of protective measures previously but erroneously thought to be adequate.

Attainment of Cleanliness

Daily tests were done over a period of six months to determine the effectiveness of mechanical and antiseptic cleanliness in reducing bacterial contamination of rooms. One series of tests was done in adjacent rooms subjected to steady and parallel usage. Cultures were taken in multiple areas of each room, with the location known only to the bacteriologist, and these were made without any preliminary preparation. Sieve sampler techniques were used for air sampling; swab and flush washing techniques were used on furniture, walls, and floors. Room 1 was then given daily the most thorough mechanical cleansing that a good workman could apply, including ceiling, walls, floors, and every item in the room. He used a detergent selected by himself at a local store. Each succeeding day for a week he bought and used a different one. His work was supervised and directed by a nurse with long experience, a known eye for dirt, and a perfectionist attitude of abhorrence for a speck of dust. In room 2, the type of cleaning supplied by the housekeeping department was continued. It should be added that the hospital has held a good public reputation locally for being a clean and neatly kept institution.

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Immediately after each room was cleaned, cultures again were taken from the same areas. Usage of both rooms continued actively throughout the day and night. Eight and 24 hours after cleaning, cultures were taken from the same areas. The rooms were similarly cleaned and tested on the second day, and the program was continued each day for seven days.

For a second week, two wards which were subject to similar usage were selected, and this experiment was repeated without variation, except for one detail. The cleaning solution used was an excellent detergent-disinfectant (Tergisyl), a concentrated solution of sodium xylene sulfonate, triethanolamine dodecyl benzene sulfonate, *o*-phenylphenol, and *p*-tertiary amylphenol. It was supplied as a 2% solution and without limitation as to amount available, both to the highly competent, especially supervised workman and to the routine workers of the housekeeping department. In subsequent one-week periods, these parallel tests of cleaning procedure and effectiveness were run on two corridors, two dressing rooms, two kitchen and dining areas, two utility rooms, two linen preparation rooms, and two operating rooms. Both test areas had the same detergent-disinfectant solution used, not only by the extremely good but also by the ordinary cleaning personnel. In fact, after the third week the detergent-disinfectant solution was adopted as the only one for every cleaning procedure in the entire hospital, not only because it was a good preparation but also in order that there might be no prejudiced factor unwittingly introduced by variation in cleaning solutions.

Analysis of these accumulated data brought out several facts convincingly. Thorough mechanical cleaning has a demonstrable, dramatic, and almost immediate effect in the reduction of bacterial contamination. This reduction progresses with daily repetition of the process. There is a slight to moderate residual effect from the cleansing over a succeeding period of several hours. Casual, superficial, and unintelligently supervised cleaning has scarcely any demonstrable beneficial effect in reducing the amount or type of bacterial flora. When an efficient detergent-disinfectant compound is added to a good mechanical cleaning process, there is an obvious residual effect that can be demonstrated bacteriologically on cultures taken as long as eight hours after previous cleaning. From these many weeks of comparative studies, there emerged an important facet of truth: By a procedure of frequently repeated, intelligently directed, and vigorously applied mechanical effort in combination with a good detergent-disinfectant, any surface or area whatever can be rendered clean or even sterile.

There were additional observations. The wards were the dirtiest. The private rooms were the cleanest. Blankets are a constant source of contamination and will spread micro-organisms from one patient to another promptly if blankets are moved from one bed to another or if patients are put into beds that are not provided with freshly sterilized, clean blankets.[2] So also will contamination be transferred by a blanket to an operating room if it is allowed to go with the patient from his bed to that room. One can render washed bankets uniformly sterile by addition of a 2% concentration of *o*-phenylphenol and *p*-tertiary amylphenol (Amphyl) to the final rinse of the laundry washing cycle. Ordinary mops and cloth rags are little more than culture mediums for bacteria unless they are frequently and thoroughly cleansed in a detergent and disinfecting solution. Straw brooms and dry mops and dusters, like ordinary vacuum cleaners, are essentially dispersing agents for bacteria, and the use of all of these items should be prohibited in hospitals.

Although hot water plus a good detergent-disinfectant makes an excellent cleaning solution, it has been shown to become infected with viable organisms unless the solution is changed frequently enough to avoid development of a dirty appearance. Laundry hampers, as used in standard practice, are filthy, but they can be readily sterilized before being used to receive clean laundry. The best routine is the requirement that they be turned upside down and washed out with a detergent-disinfectant solution, but laundry workers will not cooperate with this regulation except when forced to it. Additionally, the hampers should be lined with paper before receiving clean laundry for return from the laundry department. The latter regulation can be enforced without difficulty. The chutes down which the laundry is dumped in Huggins Hospital, and presumably in most hospitals,[3] are heavily infected. If doors on two floors are opened simultaneously, the chutes become wind tunnels which blow contaminated air out through the porthole doors into the corridors. Vertical laundry chutes are a menace bacteriologically for which no satisfactory solution has been found.

Abundant evidence from hundreds of cultures shows that, where there are large numbers of patients present and people in attendance to these patients, the level of air pollution rises, and markedly in some instances. Regardless of how intensive the clean-up effort is or of the observation that cultures taken immediately after a thorough clean-up show the number of organisms present to be reduced substantially, there is a rapid and stepwise build-back of the total numbers recoverable from exposed surfaces in a room after a period of time. The evidence also indicates clearly that air pollution is related to the amount of dust about any one area and that air pollution can be greatly reduced by effective housecleaning. It is hard to reduce and maintain in reduced form the number of organisms present as fomites when there are patients and visitors congregated in an area. However, it is possible to reduce the number of airborne organisms by the removal of dust, and, by so doing, one removes a vehicle for transportation of these organisms widely throughout a room. When people in ordinary clothing and uniforms are admitted, evidence of contamination both of the surfaces and of air rapidly rises in a room, no matter how carefully it has been cleaned previously or how short a time beforehand the cleaning was done. The rate and amount of rise are proportional to the amount of visible dirt and dust and to the volume of usage.

Maintenance of Cleanliness

The subjects which must be considered in maintenance of cleanliness are personnel, room air, masks, clothing, shoes, equipment, supplies, and procedures. A series of experiments were run in a room which had been brought previously to near-sterile conditions by an ultimate type of cleaning procedure, to which only filtered noncontaminated air was being introduced, and it was delivered to the room at a pressure which caused all air flow from the room to be outward. Observations from these tests substantiate the following statements:

Personnel will contaminate a clean room unless they are made to obey rigidly a set of strict regulations regarding masks, freshly sterilized clothing, and shoe wrapping. Regulations for cleaning for all other personnel must be identical to those imposed on members of the actual surgical team.

Proper filters can be installed and air pumps operated for delivery of any needed amount of bacteria-free air to a sterile room under positive pressure.

Unrestrained laughter and conversation and unrestricted movement about a room cause very rapid rise in bacterial content of the air in the room. Gauze masks worn during such activity delay the rate of rise of contamination somewhat, but, after 20 minutes, levels of air pollution are about equal to those in tests where no masks were worn. Pollution by respiratory exhalation can be stopped by suitable filter-type masks. Adequate masking alone will not prevent contamination of a room and its contained air.

Sterile clothing put on by personnel and then worn into contaminated areas will immediately become contaminated and will introduce contamination into a sterile room if worn back into it. The term "contaminated area" is applicable to any hospital area, such as corridor, ward, or room, which is not subject to special supervision. The practical solution to this problem lies in provision of quick-change clothing of a type that goes on and off without passage over the head or feet.

Shoes cannot be decontaminated by any practical means. Freshly autoclaved shoes worn into a public corridor and ward, and then into a sterile room, will introduce contamination into that room. Use of protective clean coverings of the entire shoes before the wearer is admitted to a sterile area is the only way yet found for eliminating contamination thereby.

Every article of furniture or equipment that enters a sterile room from elsewhere must be decontaminated first if the room is to remain sterile. This can be done by washing, autoclaving, or appropriate wiping with detergent or antiseptic solution for a sufficient length of time.

Blankets, as they are found on the bed of a patient and in use, are often heavily contaminated and will transfer infection from bed to bed or person to person if moved. Similarly, they will transfer infection when allowed to enter a sterile room if they are on a patient as a part of the covering brought with him. Blankets can be returned uniformly from the standard laundry process in a sterile condition, if subjected to treatment with the detergent-disinfectant in the final rinse of the laundry washing cycle.

Mattresses are probably subjected to less direct patient contact than are other similar items, i. e., blankets, sheets, or pillows. Generally speaking, the bulkiness of mattresses discourages personnel from making effective efforts to clean them. Repeated random cultures were taken from mattresses in constant use, and these cultures convincingly showed that they bear large numbers of bacteria. Brisk application of a detergent-disinfectant solution with a brush, and used in amounts insufficient to cause soaking of the mattress surfaces, was many times shown to be an adequate method for reduction of bacterial counts to very low levels. No issue is here raised as to the sterilizing properties of actinic rays, but it was not possible to show consistent bacterial reduction through prolonged exposure of mattresses to sunlight. The porous nature of mattress tickings offers sufficient protection for bacteria to reduce actinic radiation effectiveness. The study of how to clean mattresses clearly demonstrated the genuine benefits to be achieved by combining a bactericidal detergent agent with diligent manual intent.

Vacuum cleaners of any except the filtration type will contaminate a clean room. Those which blow air out at one end after having passed it through a cloth bag where the dirt presumably is caught carry the same or a larger number of bacteria out the back than are brought in through the front. Vacuum cleaners which use a filter retain particulate matter very effectively and are the only types which should be used in hospitals.

Although any surface or area whatever can be brought to a state of cleanliness or even sterility by sufficient mechanical cleansing and antiseptic solution application in combination, maintenance of cleanliness or sterility of the surface and of the area depends on the type and amount of usage, the frequency of rewashing by the techniques previously enumerated, and the amount of bacteria, dust, and fomite concentration in the area where the surface is located. If ventilation and type of usage remain the same in a room, bacterial contamination of air in that room can be significantly reduced by daily application of the techniques which have been described above. Three of the very effective ways of keeping low the chance of bacterial cross infection are the use of protected dressing carts, the wearing of gloves and masks by all personnel doing dressings, and the isolation of patients harboring any infection.

Cleanliness in Operating Rooms—Base Line

Critically analytical evaluation of the cleanliness of the operating rooms, according to standards which had been established by the tests outlined in the previous section, showed that they really were not so clean as had been thought. As soon as people began to work about the rooms there was too much dust in the air. The powder on gloves was one source, and a film of this powder was making a good culture medium as it settled into crevices in corners. The inside of light fixtures contained dust particles which were shaken into the air as the lights were moved about. The undersurface of tables, adjoining surfaces on cabinets, and many other places normally thought of as having been cleaned could be shown to have fingerprints of grease spots. Dust or dirt could be taken off the wheels of the cart that brought the patient from the ward to the operating table if one sought for the dirt with a wet cloth. Anesthesia equipment and suction machines yielded positive cultures.

The use of powder in the operating rooms was stopped. The entire pavilion was subjected to the ultimate noncompromising type of mechanical cleansing that had been proved effective elsewhere, and a supervisory program was established which maintains this status each day and every day. When this had been done it was found that there was, for the first time, a base line of reliability. From this basis, studies were made which were not only consistent with common sense but also free of the frustrating, erratic irregularity and unpredictability that was characterizing attempts to study other factors before this base line of absolute room cleanliness was established.

The exact origin of a wound infection often is difficult, if not impossible, to assign. Many observations have led to suspicion that most of the sporadic infections of clean wounds at Huggins Hospital have occurred in the operating room. They have been deep seated. They have been heralded by deep cellulitis with subsequent manifestations superficially, and they have been accompanied by systemic reactions. The appearance has been different from that of a superficial or stitch abscess, which subsequently shows signs of subcutaneous involvement. In fact, nine-tenths of the contaminations that cause wound infections are believed to arise in the operating pavilion area, from entry into the wound of germs from the air, or from fomites about the personnel and patients, including those of the patient's skin. The physical areas and the number of personnel involved, therefore, are small compared to the hospital space and employees for the hospital as a whole.

Cleanliness in Operating Rooms—Air

An efficient air conditioning system can readily be made to deliver dust-free and nearly sterile air into a room at a higher pressure than the atmosphere or adjacent areas by one of several effective ways. After testing of various methods, the type of air conditioning found to be best for Huggins Hospital operating pavilion was the use of filters alone.[4] Filtered air is delivered to each of two operating rooms through a central duct in the ceiling. It is removed in part by suction outlet ducts in side walls near the floor and at a height of 7 ft. and in part by a constant flow of air outward through the crevices around the doors and into an intermediate room lying between the two operating rooms. From this entryway or intermediate room, air again passes outward under positive pressure through another set of double doors to a short passageway. The passageway connects at either end with a dressing room and on the opposite side to a public corridor.

Air sampled as it entered the operating rooms through the ducts was repeatedly demonstrated to be sterile. There was a constant flow of air outward, even when the doors were opened, and yet sporadic instances of infection were appearing and these seemed to be originating during the course of the operative procedures. Furthermore, each of these rooms carries an ultraviolet light installation with demonstrable germicidal intensity of 90% killing power at 10 minutes, at a height of 8 ft. It was shown repeatedly, by sieve samplings on many occasions, that air delivered into the rooms as above described would remain sterile when the room was not in use. As soon as usage started, the bacterial counts would gradually rise to levels which were undesirable.

Practically speaking, infection or contamination of a clean room that is receiving only clean air into it is introduced by exhalations of personnel entering the room and by fomites from the clothing, shoes, or objects that people entering the room bring with them. Much study of the air filtration problem in reference to personnel has been done in the mining and fumigating industries.[5] In these industries the problem is largely one of protecting the personnel from the atmosphere or environment. They are concerned with taking fumes and particulate matter out of the air which is to be inhaled by the personnel.

The problem is reversed in surgery, and one is concerned mainly with protection of the atmosphere against germs exhaled by personnel in order that it may not be contaminated and transmit infection to the patient or his open wound. For many years, the traditional gauze mask has been worn in recognition of this problem and as one attempt at solution. Unfortunately, gauze masks are of negligible efficiency insofar as protection of room air against bacteria contamination is concerned. Doubling the masks and changing them at frequent intervals, such as once an hour, was tried with the thought that this might be a tolerable answer. There is a discernible barrier effect directly in front of a dry gauze mask and, more noticeably, in front of doubled dry gauze masks for short periods of time after they are put on. This protective effect diminishes rapidly as the mask becomes moist, is related to the amount of talking or forcefulness of breathing, and is down to less than 10% efficiency after 10 minutes if the wearer is also talking. However, there is a billowing-out effect around the sides of these masks from the beginning of wearing, no matter how carefully they are applied. With use of sieve sampler techniques one can gather large numbers of bacterial colonies from air emerging beneath the sides of these masks from the moment that they are put on.

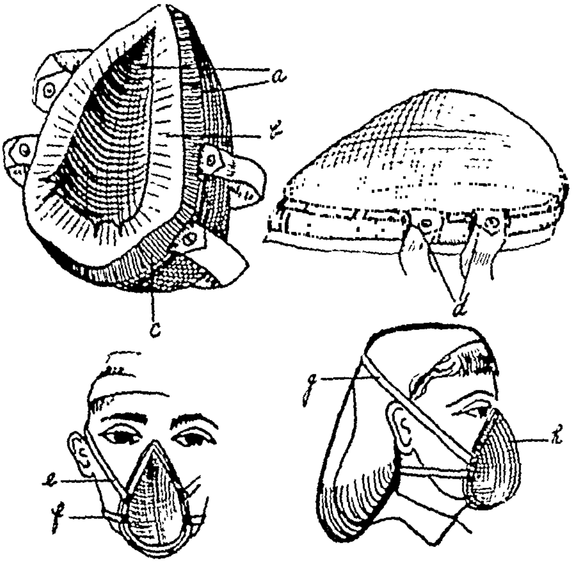

Fig. 1.—Fitted filter masks: *a*, inner and outer wire screening, *b*, adapter ring of autoclavable fiber foams, *c*, spring-constant adaptability to facial contours, *d*, snap-on elastic structural holders, *e*, elastic headband, *f*, detachable elastic band, g, best positions for wearing bands for holding mask, *h*, mask formed to maintain complete central vision.

Therefore, an extended study was made of the masking problem in search of an efficient answer that would also be a comfortable one for the wearer. A mask made as a common gauze mask and simply containing a filter instead of a piece of gauze is really little better than the gauze. It will stop the direct passage of bacteria through the mask, but the billowing out effect is unchanged. In fact, the situation can be made even worse than by a gauze mask if one chooses a completely impervious mask and substance to put in front of the nose and mouth. The spill-over effect is then aggravated. An essential feature of any filter mask that really makes tight and nonleaking contact with the skin of the wearer is that it have an exchange reservoir. Otherwise, the wearer will have a sense of suffocation and of partially obstructed air exchange both inwardly and outwardly. A mask which is doing its job effectively will also cause moisture accumulation within the reservoir, and some means of absorbing this moisture must be provided. An interchange surface must be available of such area and characteristics that air may pass through the filter with stoppage of bacteria, but at a rate which will provide adequate oxygen availability and carbon dioxide dispersal and, simultaneously, cause neither significant suction effect during inspiration nor positive pressure effect during expiration. The mask must be light and comfortable. It must be of high efficiency at the end of many hours of use. It must be cheap enough to throw away or be completely sterilizable and easily maintained.

After testing a dozen ideas which had to be discarded and over a score of models which proved not to be good enough for one reason or another, a filter type of mask (fig. 1 and 2) was finally developed and produced which meets in practice the stringent criteria set in the preceding paragraph. Demonstrations of almost total efficiency have been accumulated on a group of different personnel, tested for periods in excess of five hours. As an outcome of the numerous tests of this type of properly fitted filter mask, it may be stated that air contamination of a room by human exhalation is at least 98% preventable and controllable by proper masking of all persons entering the room. Such masks are now available, usable, and proved in practice.

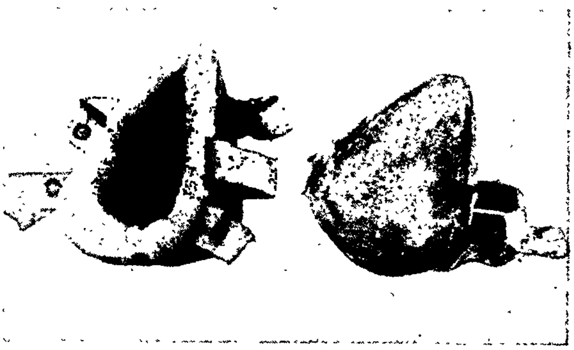

Fig. 2.—Fitted filter mask.

The patient is masked, just as are members of the operating team. Anyone entering an operating room, at any time and for any reason, should be properly masked before entering and should wear the mask during his entire stay there. This statement applies to the clean-up period after operation, insofar as trained personnel is concerned. It applies also to cleaning and maintenance help. No exceptions to wearing of proper masks should be permitted.

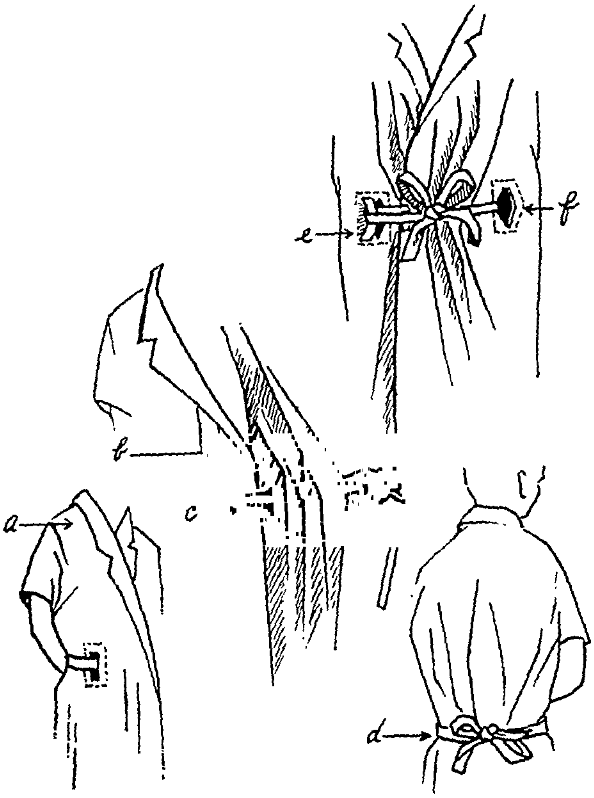

Fig. 3.—Wrap-around, quickly changed gown: *a*, reversible collar, *b*, double-breasted front coverage, *c*, pass-through opening for tie cord, *d*, tie in back, *e*, strap for front tying, *f*, pass-through opening for reverse position.

Air contamination was drastically reduced after adoption of this type of mask and insistence on its constant use by all persons entering the operating room, as shown by the following data: On July 18, cultures from operating room suite 1 showed a sieve sampler count of eight colonies on a plate, three of which were weakly hemolytic. This was the status after the room had been made ready for use during the day. Cultures from operating room suite 2 showed 23 colonies per plate after one hour of use. In the entryway leading to the operating rooms, a count of 17 colonies per plate was found. In the nurses' dressing room on the same morning, the count was 53 colonies on a Petri plate. On July 22, efficient filter masks were worn and cultures from suite 1 showed six colonies and those from suite 2 showed three colonies per plate after an hour of use. The entryway to the operating rooms showed nine colonies. The doctors' dressing room showed 55 colonies. In other words, there was a noticeably good effect from the adoption of efficient filter masks, but a condition of full sterility was still further from attainment than seemed desirable and possible.

Cleanliness in Operating Rooms—Clothing

A more careful scrutiny was therefore made of clothing. A freshly autoclaved gown was put on and worn for the five minutes required to change a dressing on a patient known to have an infection with Proteus organisms. Care was taken not to touch the gown with the gloved hands, and reasonable care was exercised in protecting the gown from contact with the bed, in the same manner as when changing a dressing while wearing street clothes or operating room clothes. Cultures taken immediately afterward from this gown yielded Proteus organisms. Culture was taken from a clean operating room uniform and subsequently showed no growth. The uniform was then put on and worn for 45 minutes in the course of routine early morning rounds (presumably clean), before scrub-up for the first operation. No dressings were taken down. The hands were washed each time after a patient had been examined. The clothing was known to have come in contact with several beds, but only in the manner that is normal in the making of rounds. At the end of rounds, the uniform was taken off and cultures taken. These showed contamination of the uniform by a wide variety of mixed organisms. Additional tests of a similar nature were carried out on subsequent days.

Proof was accumulated that all clothing worn in a nonclean room, for however brief a time, is almost surely contaminated by fomites and that such clothing will introduce contamination into a clean room if worn into that room. For example, a clean nurse's gown was put on and worn for the two minutes required for the nurse to leave the operating pavilion, cross a public hallway, and enter a recovery room for delivery of a flask of solution. She returned immediately to the operating pavilion and the scrub gown was shown by culture to be contaminated by a mixture of bacteria. The bottoms of men's trousers are among the worst sources of bacterial spread in this manner. Not only are they likely to be soiled by passage over filthy shoes, but they flap with walking and their nearness to shoes, the floor, and the dust usually present on a floor makes them an infection hazard. After starting these tests, we rapidly realized that the frequent trips in and out of an operating pavilion for doing of chores and errands, as is so common a practice and need with physicians and nurses, is hazardous from the standpoint of contaminating an operating room.

Thereafter, a long series of studies was done with respect to how the obvious inconvenience of the necessary change of clothing might be overcome in order to be wearing freshly sterilized clothing on each entry or reentry of the operating room and to fulfill the strict requirements of operating room area protection. This element of protection is essential in respect to clothing worn by personnel of all types, whether senior surgeon, intern, pavilion supervisor, scrub nurse, anesthetist, instrument maid, cleaning man, or anyone else, without exception. We sought to devise clothing that would permit quick change with little loss of time and scarcely any risk of contamination in the process of changing. Such a garment should be quickly resterilizable, reasonably good-looking, and comfortably acceptable to those who would need to wear it. After a succession of 18 trials and models, a sexless, sizeless, sideless, quick-change, double-breasted gown was developed that seems to meet the above requirements satisfactorily (fig. 3 and 4). One garment can be taken off and a new one put on within 30 seconds. It provides protection against exposure, ties in the back, and has no need to be turned in respect to sleeves, as both sides are identical. It will overlap in either direction in recognition of the different habits of men and women in putting on garments, and it is given rough-dry laundering to save ironing expense. This is the only practical garment yet found for wear in clean rooms where frequent exit and reentry are necessary. A freshly sterilized gown of this type is put on for each reentry of an operating room.

Cleanliness in Operating Rooms—Shoes

Shoes are an article of clothing, and all statements previously made about clothing in general are applicable to shoes in particular. Additionally, shoes present surfaces and are specifically subject to the rules for attaining cleanliness outlined in the early part of this paper in respect to the cleaning of rooms and the furniture within rooms. By nature of their function, shoes are always dirty, from a bacteriological standpoint, and 10 minutes' time spent in mechanical scrubbing with a good disinfectant-detergent is the only method discovered that will suitably clean them. This fact makes decontamination of shoes, before reentry to a clean room in active use, impractical and impossible of attainment.

A shoe that was cultured without having any treatment at all showed a massive growth of a mixed flora of bacteria. A second shoe that was soaked in a 10% phenol detergent solution for one minute showed a relatively high number of bacteria growing out from a swab passed over the sole. The same was true of another shoe that had been treated with pure phenol. When shoes that had been soaked for one minute in each of these strengths of solutions were scrubbed vigorously with a brush for 30 seconds, the number of viable organisms remaining dropped off markedly. However, 10 minutes of vigorous mechanical scrubbing was necessary in order to render a previously dirty shoe surface sterile to culture. It is of interest to note that the antiseptic detergent solutions were fully active in their bactericidal effect, insofar as they were able to come into direct contact with organisms present. Where there is some protective effect afforded through the presence of a layer of dirt, this bactericidal action is inhibited and organisms are readily grown on culture mediums. It is now apparent that, in order to have an effective shoe-soaking arrangement, one would need to set up a brush or series of brushes over which the shoe could be scrubbed while being wetted with an antiseptic solution and that one would need to carry out this activity for 10 minutes if he expected to produce a sterile shoe surface. There is nothing really surprising in the finding, except that anyone should ever have thought that simply wiping

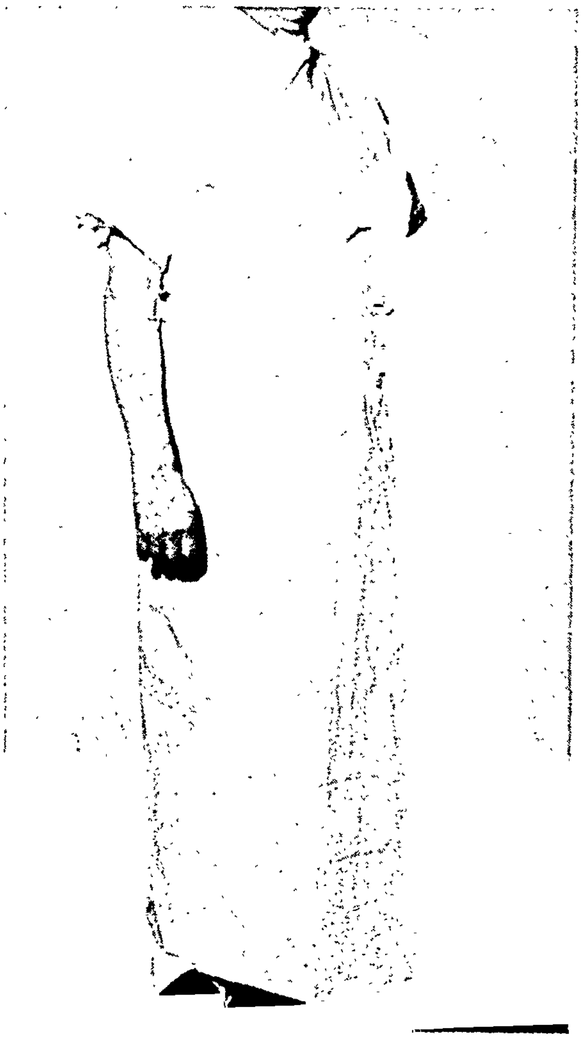

Fig. 4.—Wrap-around, quickly changed gown.

ordinary shoes with a detergent cloth would decontaminate them. No one should believe, any longer, that a surgeon's hands can be sterilized by dipping them in a detergent solution or even by washing them for a minute or two with some such solution. Every serious student of the subject knows that a good, enthusiastically applied, 10-minute mechanical scrubbing is necessary to clean a surgeon's hands. Why should it be supposed that his shoes would require much less?

This intensive study of the problem of protecting the operating suite against contamination from shoes worn by personnel yielded reaffirmation of the axiom that mechanical energy must be expended on the surface of whatever is to be cleaned.

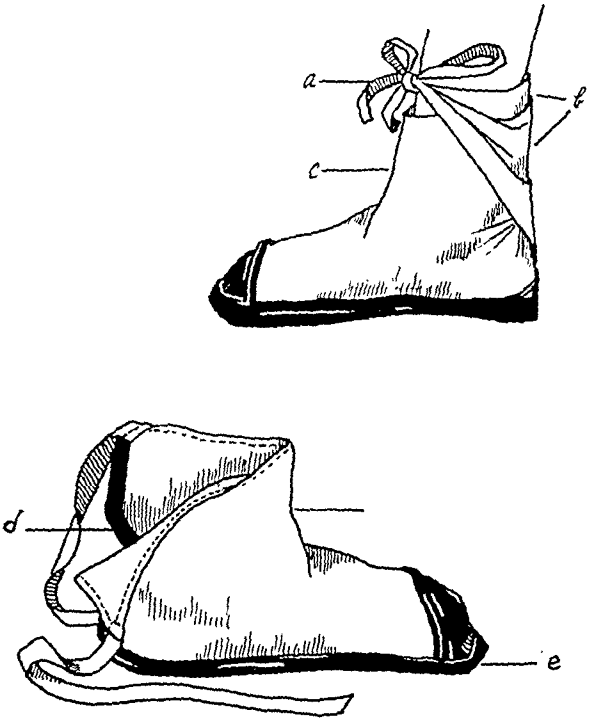

Fig. 5.—Conductive, protective bootie: *a*, front tie, *b*, wrap-around for complete coverage, *c*, weight to cover both shoe and sock, *d*, rubber strap conductor coming to skin contact, *e*, conductive rubber soles.

Phenolated detergents, chlorinating compounds, iodine, benzalkonium chloride, in whatever strength of tincture, formulation, or solution, all are ineffective unless combined with mechanical effort.

Attention was turned to other methods. After extensive testing and modeling, a washable, flexible, slip-on, wrap-around, cloth-top, conductive rubber-soled bootie was developed and produced that meets all requirements (fig. 5 and 6). It is worn by everyone while they are in the operating rooms or adjacent rooms. They may be worn outside of the operating pavilion at will but must be discarded and a freshly cleaned pair put on before reentry is permitted. They may be worn out of the operating rooms and into the dressing rooms only without being changed before reentry. This is a satisfactory compromise with practicality, in that the soles of the booties are readily cleansed by wiping them on a blanket soaked in detergent antiseptic solution after such brief exposure to a relatively clean area.

Comment

What was true in other areas is true in this: 1. An operating pavilion can be cleaned up by mechanical effort, application of detergents and antiseptic solutions, and persistent attention to details of care. 2. An area so cleaned will remain clean until contamination is introduced into it. 3. Personnel can so conduct themselves in respect to the masks, clothing, and shoes worn that they need not introduce infection to a room by virtue of their presence in the room. 4. The air introduced into a room through the conditioning system can be delivered sterile or nearly so. 5. All inanimate objects taken into a room can be delivered there in clean or sterile form. In other words, the problem of maintaining sterility, or conditions so nearly sterile that they can be regarded as totally clean, is a soluble one in respect to a given room. The solution can be kept within economically practical bounds for a relatively small area, such as an operating pavilion, because of the geographical confinement and because of the high level of intelligence, understanding of need for cleanliness, and dedication that characterizes the attitudes of most persons who work about operating pavilions.

The following absolutes of sanitation must prevail and are the criteria for attaining and maintaining a bacteria-free operating room. There is an inner zone, the operating room itself, where uncompromisingly rigid and total requirements of sanitation are constantly in effect. Every item admitted to this environment must be as nearly germ free as it is possible to make it. An interchange area exists inside which all aseptic criteria are fulfilled: the shoes are wrapped in booties, the clothing is clean, and a filter mask is worn. The interchange area itself, where these conditions are established on passing inward, contains the scrub-up sink. Impervious aprons are required during scrub-up to prevent wetting of the clothing with droplets from scrub brushes.

A zone lies outside of the interchange area where complete cleanliness in reference to the room and floor and furniture is maintained. But here masks are not worn. Booties may or may not be on. Pavilion clothing may be worn or not. These areas are the dressing rooms and the entryways to these rooms and to the interchange zone. They lie outside the interchange zone but within the operating room pavilion.

Outside of the pavilion is the rest of the hospital. From the standpoint of protection against germs, the area outside the pavilion is outside the pale and includes everything and everybody.

On the floor of the interchange area there is a blanket 6 ft. wide extending from wall to wall; this is put down freshly washed each day and is soaked in a disinfectant detergent solution. When a transfer cart brings a patient to this zone, the cart is stopped on the blanket and the patient is transferred to the operating room cart. If a recovery room cart is taken into the operating room itself, the cart is first washed with antiseptic solution, including the wheels and tires. The clothing and covering which the patient is to wear in the operating room are put on him in the interchange area.

Personnel put on their masks in the interchange area or outside it. They put on their booties from the sterile supply while sitting on stools on the detergent–antiseptic–soaked blanket in the interchange area, so that the booties present over-all sterile surfaces from the time the protected area is entered. If a person must leave the protected area temporarily to go into a dressing room, the gown may be worn back into the protected area, as may also the booties if their soles are wiped off on the wetted blanket. This is germicidally effective because there is little dirt or dust in the air or on the floors of the dressing room or operating pavilion. The booties have been washed and are always thoroughly clean prior to the current wearing, and the soles are therefore readily cleansed to meet practical requirements.

Although such conditions can be sought and temporarily achieved in other departments of the hospital, such as wards, kitchen, bathrooms, laundry, and examination rooms, one must concede that there are not enough people with requisite supervisory skill or dedication to work for fulfillment of these requirements beyond a limited zone. There is a difference between what can be proved and what can be done, unless one is able to provide total, constant supervision. Fortunately, the area of a hospital in which such exacting standards of performance must be met is the same one where they can be maintained in ways that are practical, economical, and reasonable.

A concept of this whole problem of operating room protection is as follows: There is a certain area, which is the operating room itself, where ideal performance is a minimum requirement. There is an outer area, the public area, where contamination is universal and controllable only within limits. Between these extremes, there must be degrees of sterility which increase as one moves inward but where some leeway in the intermediate zone is necessary.

The practical effect of willingness and ability to carry out this program on a daily basis is shown by the following reports on cultures taken by a bacteriologist, without prior announcement to anyone that he had plans to take them and at the end of a period of time in which two operating rooms, the entryways, the interchange zone, and the dressing rooms and associated passageways had been steadily in use for four hours. Five-minute air samples were taken by a sieve sampler technique. Operating room 1 showed two colonies. Operating room 2 showed one colony. The scrub room or separation room between the two operating rooms showed 14 colonies. Eleven colonies were obtained in the hallway between the dressing rooms and 20 colonies in the nurses' dressing room. At the same hour, for purposes of comparison, culture samples were taken from a public hallway outside the operating pavilion, and this showed 49 colonies, 15 of which were potently hemolytic and 2 of which were soil organisms. A plate exposed in the men's ward showed the presence of 61 colonies, of which 12 were hemolytic, 6 were potent hemolizers, and 1 was a soil organism.

Fig. 6.—Conductive, protective bootie.

The skin of a patient can be cleansed in the same manner as can the skin on the hands of a member of the operating team. Nothing less than a 10-minute, enthusiastically applied, mechanical washing with detergent soap solution and water, followed by a process of drying and application of antiseptic solution, will suffice. The proposition that skin on the hands of personnel should be covered by thin, sterile, impervious material, such as rubber or plastic gloves, has been accepted and universally applied for three generations. The skin of the patient has not been similarly treated and has remained a source of risk to wounds, even though precautions to cover skin margins and subcutaneous tissues, and other protective measures, were taken.

Recently, a thin, transparent, autoclavable, plastic film material (Vi-Drape surgical film) has become commercially available. It is capable of being made adherent to the skin by the application of a spray-on adhesive bond (Vi-Hesive surgical adherent).

The adhesive bond is first sprayed on slowly at a distance of 10-12 in. over the whole scrubbed area and allowed to dry for 30 to 45 seconds, until tacky to touch. The sterile film is then held over the area, lowered first over the areas of intended incision, and then molded onto the skin over the whole operative site. The usual surgical drape is then applied.

This technique has become an integral part of the draping and preparatory procedures to further isolate the wound from its environment prior to making the skin incision, which is made through the plastic material. The latter remains intimately adherent to the skin margins, and the skin, although visible, is completely occluded from the operative area for the duration of the procedure. The adhesive bond lasts for at least many hours, and protection against contamination of the operative area from the skin can be maintained indefinitely by the sterile impervious plastic membrane.

These materials have now been used in over 300 surgical cases. They are in no sense a substitute for scrupulous and meticulous skin preparation but are an added protection of the patient's skin, equal to that afforded by gloves on the hands of operating personnel.

Summary and Conclusions

Extensive studies of sources of infections in hospitals led to recognition of the following fundamental facts: Frequently repeated, intelligently applied, mechanical effort in combination with a good disinfectant-detergent will clean any area. Maintenance of cleanliness or sterility of the surface depends on the type and amount of usage, the frequency of rewashing by these techniques, and the amount of bacteria, dust, and fomite contamination.

If ventilation and type of usage remain the same, bacterial contamination of air in a room can be significantly reduced by daily application of proper cleaning techniques. An efficient air conditioning system can readily be made to deliver dust-free, nearly sterile air into a room under positive pressure. Such air, delivered into a clean room, will remain nearly sterile indefinitely, unless contaminated by introduction of infection. This is introduced by exhalations of personnel entering the room and by fomites from clothing, shoes, or objects brought in.

Air contamination of a room by human exhalation is at least 98% preventable and controllable by proper filter masking of all people entering the room.

All clothing worn in a nonclean room, for however brief a time, is almost surely contaminated and will introduce contamination into a clean room. Because of problems of time consumed, inertia, and contamination from passage over unclean areas of trousers or slip-on garments, double-breasted, wrap-around, quick-change, lace-tying gowns are the only practical answer yet found for wear in clean rooms where frequent exit and reentry are necessary. A freshly sterilized garment of this type must be used for each reentry of a clean room. If used where there are flammable gases, the garment must be constructed of a material which will not produce static electricity. All statements made about clothing are applicable to shoes. Quickly donned, temporary shoe coverings are a practical solution to attainment of clean footing for all personnel using a clean room. Fresh coverings must be used each time a clean area is to be entered. If flammable gases are used in the clean room, the shoe coverings must have conductive soles as an integral part of their construction, and these soles, as well as the tops of the coverings, must be sterilizable by autoclaving. Critically competent supervision and working personnel with attitudes of dedication to maintenance of cleanliness are necessary.

Nine-tenths of the causes of wound infections are believed to arise in the operating pavilion area from entry into the wound of germs from the air or from fomites about the personnel and patient, including those of the patient's skin. The geographical area and the number of personnel involved, therefore, are small compared to the hospital space and employees for the hospital as a whole. A sterile skin surface can be achieved by 10 minutes of diligent scrubbing with germicidal detergent soap and water. The sterility of this surface can be maintained indefinitely by the proper application of an adherent transparent plastic film.

A room which looks clean, smells clean, and feels clean is most likely to be clean and to be proved clean also when subjected to critical testing for bacterial and particulate matter content. For nine-tenths of the hospital, a good housekeeper with an eye for dirt and an ability to get it removed is a better investment than complicated bacteriological testing equipment and routines. For the other one-tenth of the hospital area, meaning essentially the operating pavilion and the nursery, standards, controls, and fulfillment must be of the ultimate type from which no appeal for leniency is tolerable.

The detergent-disinfectant uesd in this study was supplied as Tergisyl and the *o*-phenylphenol—*p*-tertiary amylphenol as Amphyl by the Lehn & Fink Products Corporation, Bloomfield, N. J. The plastic surgical film material was supplied as Vi-Drape surgical film and the spray-on adhesive bond as Vi-Hesive surgical adherent by the Aeroplast Corporation, Dayton, Ohio.

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EXPERIMENTAL PANCREATITIS–RECENT CONTRIBUTIONS

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The fact that pancreatitis and disease of the biliary tract frequently occur together has led to many types of experiment on possible interactions between bile and pancreatic juice. Especially tempting is the hypothesis that some constituent in bile, in tissue juices, or in inflammatory exudates is capable of activating pancreatic juice and so causing the familiar picture of hemorrhagic necrosis of the pancreas. There is also a tendency to assume that the appearance of abnormal enzymes in the circulation during pancreatitis means that they were produced in the pancreas and are responsible for the symptoms of shock. In reality, the injurious factor in pancreatitis has not yet been identified, and the role played by circulating proteases remains to be explained.

Many methods for producing experimental pancreatitis are available, and descriptions of new methods are constantly appearing. All forms of experimental pancreatitis bear some resemblance, in gross and microscopic pathology, to certain forms of the human disease. This resemblance is best interpreted as indicating that the reaction of the pancreas to injury is rather stereotyped, differences in the pathological picture being due more to the rate and amount of injury than to the nature of the injurious agent. For this reason, caution must be used in arguing from experimental pancreatitis to the pathogenesis of the human disease.

Several recent reviews systematically survey the literature on experimental pancreatitis.[1] This paper will not attempt to duplicate these efforts but will deal only with selected topics which invite evaluation in the light of recently acquired evidence.

The Bile Factor

The frequent association between disease of the biliary tract and pancreatitis is a well-documented clinical fact. Of the various theories which attempt to explain this association, that of Opie, postulating reflux of bile into the pancreatic duct through a common channel, is dominant in terms of the number of adherents it commands. That a communication frequently exists between the common bile duct and the major pancreatic duct of human subjects has been clearly established on the basis of both anatomic dissections and operative and T-tube cholangiography. However, the question of whether bile actually refluxes through this communication under physiological or pathophysiological conditions has not yet been unequivocally answered. The pressures used during direct cholangiography are artificially high and do nothing more than demonstrate that the communication exists. The availability of intravenous cholangiography offers the opportunity of detecting biliary-pancreatic reflux under conditions of spontaneously occurring pressure. To my knowledge, no one has yet demonstrated biliary-pancreatic reflux by intravenous cholangiography in normal subjects or in patients with pancreatitis, with or without administration of opiates. A careful search for this phenomenon should be made.

Assuming that reflux of bile into the pancreatic ducts can occur, will it cause pancreatitis? Critical evaluation of the enormous literature on this subject leads to the conclusion that pancreatitis results from injection of bile into the pancreatic ducts only when the pressures used are great enough to cause mechanical rupture of the acini. It is unlikely that pressures of the magnitude required ever occur under physiological conditions.

New light on the possible role of bile in the pathogenesis of pancreatitis comes from the studies of Elliott and co-workers.[2] These investigators have

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confirmed the findings in earlier studies by showing that, when gallbladder bile was allowed to flow into the pancreatic duct under relatively low pressure (40 cm. H_2O), little entered the gland and no significant damage resulted. However, if the bile was incubated with pancreatic juice of high enzyme content or with trypsin for 12 hours before allowing it to flow into the pancreatic duct, then large amounts entered (18 to 30 ml. in one-half hour) and lethal hemorrhagic necrosis ensued. Presumably, the proteolytic enzymes of pancreatic juice degrade a substance in bile (perhaps mucoprotein) which modifies the ability of bile to penetrate and injure the pancreas. As early as 1906, Flexner[3] showed that the injurious agent in bile is bile acid and that it is more effective in producing pancreatic damage when freed of the protein of bile. Whether such an interaction of bile and pancreatic juice can occur in the intact organism remains problematic.

Pressures in the Pancreatic and Biliary Ducts

Most of the earlier studies on pressures in the pancreatic and biliary ducts were concerned with so-called secretory pressures, that is, the vertical height to which fluid would rise in a tube connected to a cannula occluding the duct. Menguy and associates[4] have recently devised a method for making serial pressure measurements in the physiologically intact pancreatic and biliary ducts of unanesthetized dogs over periods of many months. These studies have shown that, even during fasting, remarkably high pressures are present, the mean value for the pancreatic duct being 14 cm. H_2O and for the biliary duct 7 cm. Stimulation of the flow of juices in these ducts by meals or by injection of secretin or dehydrocholic acid usually, but by no means always, caused a modest increase in pressure.

Since large increases in flow rate can occur with little or no increase in pressure, it is valid to deduce that resistance to flow is subject to marked physiological adjustment. Conversely, it has been clearly demonstrated that when outflow resistance is increased no decrease in rate of flow occurs until the outflow resistance approaches the level which will produce complete cessation of flow.[5] Thus, unlike a water tap in which flow is inversely proportional to outflow resistance, the pancreatic gland is capable of increasing intraductal pressure in response to increased outflow resistance so as to maintain flow constant. Whether the increased intraductal pressure which results from partial obstruction to outflow can be sustained for long periods of time and, if so, whether it would lead to damage to the gland has not yet been studied.

Of special interest in the studies of Menguy and associates was the demonstration that introduction of alcohol into the duodenum caused a sustained rise in pressure in the pancreatic duct. The association between acute and chronic alcoholism and pancreatitis is evident clinically, and information about the physiological effects of alcohol on the pancreas is, therefore, important.

Vascular Factors

The recent studies of Thal and co-workers[6] have convincingly reasserted the effectiveness of ischemia in producing fulminant lethal hemorrhagic pancreatitis. When the capillaries and venules of the pancreas were made to undergo thrombosis by the local Shwartzman or Arthus phenomenon or were severely constricted by introduction of staphylococcic toxin through the duct, typical diffuse hemorrhagic necrosis rapidly ensued.

By contrast, it has once again been demonstrated, in the studies of Menguy and associates,[7] that ligation of the major arteries and veins of the pancreas produced only small patches of necrosis, although when such ligation was combined with obstruction of the ducts the severity of injury was increased. The severe hemorrhagic pancreatitis which Pfeffer and co-workers[8] produced by creating a closed loop obstruction of the portion of the duodenum where the pancreatic ducts enter is another example of the cooperation of obstructive and ischemic factors.

Two principles emerge. First, because of the richness of the collateral blood supply to the pancreas, ischemia of the tissue sufficiently severe to produce necrosis, when acting alone, can only be achieved by stopping the flow of blood in the smallest vessels. Second, lesser degrees of ischemia can greatly enhance the damaging effect of other factors such as obstruction of the duct.

Pancreatic Proteases and Lesions of Pancreatitis

It has long been assumed that the proteolytic enzymes of pancreatic tissue and of pancreatic juice play an important role in producing the lesions of pancreatitis. It is well established that both trypsin and chymotrypsin, when present in sufficiently high concentration, are capable of producing severe tissue damage at the site of their local injection. A prominent feature of this damage is necrosis of the walls of vessels and associated tissue hemorrhage. The hemorrhage with vascular necrosis seen in pancreatitis is comparable to that produced by injection of the pure enzymes, and this similarity is, to date, the strongest evidence available implicating these enzymes in the pathogenesis of the disease.

When trypsin or chymotrypsin is injected intravenously in a sufficiently large amount, death associated with shock occurs. The pathogenesis of this effect is uncertain, although there is evidence to suggest that it is due to release of vasoactive substances, such as histamine. Similarly, the damaging action of proteolytic enzymes injected into tissues may be dependent on local release of vasoactive substances which lead to ischemia.[9] It is often assumed that the shock which sometimes occurs in patients with pancreatitis is due to release of active proteases into the blood stream. Although many attempts have been made to demonstrate active pancreatic protease in the blood in both experimental and clinical pancreatitis, no convincing evidence for their presence has been adduced. Blood plasma has powerful antitryptic and antichymotryptic activity, and the amount of enzyme present in the blood must be great enough to overcome this inhibition before it can be measured.

Several groups of investigators have demonstrated a circulating protease in experimentally induced pancreatitis,[10] but it has not been proved that this protease is actually of pancreatic origin. Blood contains a proteolytic enzyme, plasmin, present mainly as an inactive precursor, plasminogen, and the blood concentration of both the precursor and the enzyme rise after a wide variety of nonspecific stresses, such as surgical operation.[11] Plasminogen may be converted to plasmin by a kinase of bacterial origin, streptokinase, which is incapable of activating pancreatic proteases. It has recently been demonstrated that there is elevation of the concentration of plasminogen as well as of an active protease with the properties of plasmin in animals with experimentally induced pancreatitis.[12]

In addition to their hydrolytic action on peptide bonds, pancreatic proteases have been shown to be capable of hydrolyzing a variety of amino acid esters and amides. The possibility of using these synthetic substances for detecting pancreatic proteases in the blood of patients with pancreatitis is receiving attention currently. Because blood plasma inhibits the esterase action of trypsin and chymotrypsin less than their protease action, it is possible to detect these enzymes by esterase measurements in the blood of animals after intravenous injection of amounts which produce neither shock nor death.[13] These methods offer great promise for elucidation of the pathogenesis of the experimentally produced and the clinical disease. However, these synthetic substrates are attacked by enzymes other than those of pancreatic origin. For example, arginine esters and arginine amides are split by trypsin, but they are also attacked by plasmin, thrombin, and tissue cathepsins.[14] In order to prove that elevation of the rate of splitting of such a substrate is due to pancreatic protease, it will be necessary to employ a variety of criteria, such as relative rate of splitting of different substrates and pH optimums. The recent report that patients with pancreatitis show an increase in the blood level of an enzyme which hydrolyzes benzoyl arginine amide[15] must be viewed in this light.

The proteolytic enzymes of the pancreas, trypsin and chymotrypsin, are secreted into the pancreatic juice in the form of inactive precursors, trypsinogen and chymotrypsinogen. An enzyme secreted by the intestinal mucosa, enterokinase, converts trypsinogen to trypsin. Once this process has begun, it proceeds rapidly because it is autocatalytic in nature, that is, trypsin catalyzes the conversion of trypsinogen to trypsin. In addition, the transformation of chymotrypsinogen to chymotrypsin is accomplished by trypsin, and this reaction is not autocatalytic.

In the literature on the pathogenesis of pancreatitis, one frequently encounters the statement that the conversion of pancreatic proteases from their inactive precursor forms to the active enzymes can be accomplished by a variety of agents other than enterokinase, including bile, tissue juices, and inflammatory exudates. It is thus assumed that if these enzyme precursors find their way into intercellular sites they will rapidly become activated.

This problem has recently been studied in detail. Pancreatic juice was collected from the ducts of unanesthetized rats and dogs with food acting as the stimulus for secretion. It was found that these juices invariably contained a trace of active protease but that this usually represented less than 1% of the potential proteolytic activity which could be released by activation with enterokinase. When tested on synthetic substrates which are attacked by trypsin, this spontaneously appearing active protease did not produce any hydrolysis. Another indication that this spontaneously active protease was not trypsin was the fact that when minute amounts of crystalline trypsin, equivalent in proteolytic activity to the spontaneously appearing protease, were added to the juice full activation, as great as with enterokinase, occurred within a few minutes.

A variety of substances were added to pancreatic juice to test their ability to produce activation of protease. Rat hepatic bile, dog gallbladder bile, 2% solution of sodium cholate, inflammatory exudate produced by injection of turpentine into the thoracic cavity of rats, an aqueous extract of human leukocytes, plasmin, thrombin, and streptokinase were tested. None of these substances, with the exception of thrombin, produced any increase in the rate of appearance of active protease over that seen with pancreatic juice alone during periods of observation up to 24 hours. The weak activating action of the thrombin preparation could be fully accounted for by its content of calcium. Calcium salts in a concentration of 0.05 M caused complete activation of pancreatic protease. The activation by calcium salts, which had been extensively studied by a number of earlier workers, is characterized by a long lag phase, during which only slight acceleration of activation occurs, followed by very rapid, presumably autocatalytic, total activation.

Unactivated pancreatic juice was injected into the thoracic or abdominal cavity of rats, and samples of it were periodically removed for assay of proteolytic activity. The increase in concentration of active protease over a six-hour period was slower than that of a similar solution incubated in vitro at 37 C.

These results offer no support for the view that tissue juices, bile, or inflammatory exudates are capable of activating pancreatic protease. The important problem of whether pancreatic proteases become activated during the course of clinical or experimental pancreatitis and, if so, how this is brought about, awaits a definitive answer.

Conclusions

The experimentalist could easily be beguiled into thinking that he knows a great deal about the etiology of clinical pancreatitis because he can so easily mimic the disease in animals. Actually, what is known is that there are a number of factors which can cause injury to the pancreas and that when this gland is injured it reacts in certain characteristic ways. The identification of the injurious factor or factors in the clinical disease has not yet been accomplished.

The experimentalist can be equally naive in regard to the pathogenesis of the disease. It is plausible and useful to hypothesize that injury to pancreatic acinar cells causes release of enzymes into tissue spaces and that these enzymes then produce characteristic types of damage and reaction. While this hypothesis is almost certainly valid in a general sense, its intimate details are but poorly understood.

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NEW WORLDS AWAIT SENIOR CITIZENS.—From the accent on youth the time has come to recognize and develop the concept of maturity. From being sickness-oriented there is need for becoming positive-health-minded. From emphasis on chronological age the more accurate estimate of an individual is his biological or fitness performance capacity. From limiting the medical focus to the requirements of the individual there is a broader aspect, the family and the impact of disease on its group vitality. Acute diseases are now relatively less important than long term disorders and the necessity for their prompt control. Finally, the barriers of age retirement must be re-examined, and thought now should be directed to the second career. Family values, happiness and security, are rooted in the vitality, health and unity of each member. The healthier each one is, the healthier the family. A kind of crisis now exists in too many families where the older members are devaluated. No one can help the elder as much as he can help himself. A whole new world awaits the senior citizen who will become alert to his potentials.—E. L. Bortz, M.D., The Emerging Twentieth Century Family, INA Conference on Family Security, Disneyland, Calif., Jan. 9-12, 1959.

MEDICAL ASPECTS OF PANCREATITIS

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The diagnosis of acute pancreatitis usually depends on the finding of a high serum amylase level in a patient with acute severe epigastric pain, abdominal tenderness, vomiting, fever, tachycardia, and leukocytosis. Increasingly exact methods of diagnosis have led to increasingly conservative methods of treatment. Therapy includes continuous aspiration of gastric contents, parenteral administration of solutions to preserve the water-electrolyte balance and combat shock, and use of antibiotics. The treatment must be adapted to the case, and surgery may be necessary. Chronic pancreatitis is usually seen in older patients after repeated attacks of acute pancreatitis, or during the progress of tuberculosis, syphilis, or hemochromatosis. Laboratory studies of the blood, especially determinations of pancreatic enzyme levels and glucose tolerance, are important in diagnosis. Chronic pancreatitis leads to diabetes, steatorrhea, and calcification, with the possibility of sudden fatal complications. Treatment is designed to eliminate, if possible, the cause of recurrences and to compensate, by means of insulin, pancreatin, and diet, for the loss of the internal and external secretions of the pancreas.

The purpose of this presentation is to discuss the medical aspects of pancreatitis. Descriptions will be given of precipitating or etiological factors, clinical manifestations, laboratory findings, diagnosis, complications, and treatment of the acute and chronic varieties of the disease.

Acute Disease—Etiology

Acute pancreatitis consists of an acute inflammation of the pancreas, the clinical manifestations of which vary with the severity of the inflammatory process as well as the extent to which the exocrine and endocrine functions of the gland are deranged. The three main varieties, edematous, hemorrhagic, and suppurative, probably represent different degrees of severity of the same process. The disease occurs in both sexes and in many instances appears to be precipitated by the ingestion of a meal, an overindulgence in alcohol, or an emotional storm. Although it is encountered most frequently in middle and late adult life, at least 40 cases have been reported in children.

All cases of acute pancreatitis do not have a common etiology. A variety of factors have been held responsible. They include obstruction of the ampulla of Vater with reflux of bile into the pancreatic duct—the "common channel theory"; obstruction of the pancreatic ducts; alcohol, ethyl and methyl; metabolic disturbances—hyperlipemia, diabetes mellitus, malnutrition, pregnancy, isoniazid administration,[1] and hyperparathyroidism[2]; trauma, due to accident, surgical manipulation, or electric shock; infection—specific infectious diseases, such as mumps and scarlet fever, as well as direct extension of inflammation from foci in the abdomen; vascular factors—obstruction of the pancreatic arterial system by atherosclerosis, essential polyangiitis, or injury from dye injected during translumbar aortography[3]; allergic factors; and neurogenic factors. Most of these have been recently reviewed in detail by Richman[4]; however, some of them will be discussed briefly in order to illustrate the varied mechanisms by which pancreatitis may develop.

Obstruction of the ampulla of Vater, a channel common to both pancreatic juice and bile, may be caused by a calculus, a plug of mucus or inflammatory debris, edema, a tumor, a parasitic worm, or spasm of the second portion of the duodenum as well as of the choledochopancreatic sphincter. The obstruction permits a reflux of bile into the pancreatic ducts, an essential feature of the "common channel" theory. However, acute pancreatitis has been encountered in the absence of an anatomically demonstrable common channel and ascribed to obstruction of the pancreatic ductal system alone as a result of a tumor, calculus, squamous metaplasia, inflammation and edema caused by a penetrating duodenal ulcer, inversion of the duodenal stump during gastric resection, or spasm of the duodenum or of the sphincter surrounding the opening of the pancreatic duct into the duodenum. In these cases the absence of an anatomically demonstrable common channel for bile and pancreatic juice has been used as evidence to eliminate the role of bile in activating the enzymes thought to be responsible for initiating the pancreatitis. Cholangiographic observations, however, suggest that reflux of bile into the pancreatic ducts can

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occur regardless of the type of anatomic arrangement of the terminal portions of the common bile and pancreatic ducts. Recently it has been postulated by Hosie and Ziffren[5] that the enzyme collagenase, present in activated pancreatic juice, may escape from the pancreatic ducts into the interstitial tissues of the pancreas and initiate a tissue reaction that transforms trypsinogen into trypsin, which in turn causes the inflammatory process.

The occurrence of attacks two to three hours after the ingestion of a heavy meal or an overindulgence in alcohol has led to the belief that these are important precipitating factors because of their ability to incite an increased secretion of pancreatic enzymes. Alcohol is thought to cause pancreatitis by causing an increased secretion of pancreatic juice against an obstruction due to spasm or edema of the papilla of Vater. The possibility of the existence in alcoholism of acute pancreatitis during the period of alcohol withdrawal after an alcoholic bout should be kept in mind. Sudden death in alcoholics due to acute pancreatitis has been reported by Dalgaard.

Acute pancreatitis has also been known to follow a direct blow to the abdomen, trauma incident to manipulation of a peptic ulcer adherent to the pancreas at laparotomy, biliary tract surgery, splenectomy, and right colectomy, as well as other operations in which the pancreas may be traumatized.

Acute Disease—Clinical Manifestations and Laboratory Findings

Clinical Manifestations.—The severity of an attack of acute pancreatitis depends on the nature of the pathological process present, i. e., edematous or hemorrhagic, as well as such complications as shock, hemorrhage, and sepsis. An attack commonly begins with a sudden pain in the epigastrium at any time of the day or at night during sleep. The pain is usually severe and constant; less often it is cramping and intermittent or dull and poorly defined. It is frequently more intense when the patient is lying supine than when he is sitting or lying on the side with his spine arched forward. Though usually originating in the epigastrium, the pain may also be experienced in other parts of the abdomen and may radiate to the back, substernal area, and flanks. Nausea and vomiting frequently occur soon after its onset. Constipation, as a result of reflex ileus, chemical peritonitis, or administered opiates, occurs more commonly than diarrhea.

A slight fever is usually present, and the pulse rate is increased, especially in the more severe cases. The blood pressure may be slightly elevated but is low in the more critical cases of patients with circulatory collapse, cyanosis, cold and clammy skin, rapid feeble pulse, and subnormal temperature.

The abdomen may be distended early as a result of ileus due to a chemical peritonitis, and peristalsis is diminished or inaudible. The administration of opiates may contribute to the ileus. Tenderness in the epigastrium is almost invariably present and is associated with rigidity. Tenderness may be elicited elsewhere in the abdomen, depending on the sites of seepage of the pancreatic juice.

A mild transient jaundice may be present as a result of associated cholangitis, obstruction of the ampulla of Vater, pressure on the common duct by an enlarged head of the pancreas, or hepatitis. Tetany due to hypocalcemia is occasionally encountered, particularly in the acute hemorrhagic form. Congestion, atelectasis, or a small pleural effusion may sometimes be detected at the base of the left lung. The latter has been ascribed to subdiaphragmatic irritation but has been found to contain significant amounts of amylase. Discoloration of the skin, varying from slate blue to mottled brownish yellow, due to ecchymosis (the color depending on the age of the extravasated blood) occasionally appears in the region of the loins (Gray-Turner sign) or of the umbilicus (Cullen's sign) at about the fifth to the seventh day of the disease. In the more severe cases of pancreatitis, a mass, often firm, fixed, and tender, may be palpable in the epigastrium or in one of the upper quadrants either early or subsequently in the course of the disease. This mass may consist of pseudocyst formation containing necrotic debris, blood, and fluid, of an abscess, or of inflamed mottled omentum studded with multiple fat necroses.

Laboratory Findings.—The leukocyte count is frequently elevated to 10,000 per cubic millimeter or more and, at times, to as high as 20,000 to 30,000 per cubic millimeter. Anemia is ordinarily absent. The concentration of serum amylase is usually increased to more than four to six times normal early in the attack, but no constant relationship exists between the elevation of the amylase level and the severity of the illness. It returns to normal within three to four days in uncomplicated cases. Persistent elevations indicate a continuation, extension, or progression of the process. The concentration of amylase in the peritoneal fluid obtained by abdominal paracentesis has been found to be increased and to remain elevated after the concentration in the blood has returned to normal. The appearance of the aspirated fluid may furnish some information as to the type of pancreatitis present, a yellow, turbid fluid indicating the edematous and a reddish brown color indicating the hemorrhagic form. The concentration of amylase in 24-hour collections of urine is frequently elevated and may remain elevated for longer periods than that in the serum after the acute attack has subsided. The concentration of serum lipase may be increased early in the attack and remain elevated after the serum amylase level has returned to normal. Nardi and Lees[6] recently have found the serum trypsin level to be elevated in patients with acute pancreatitis; they believe this determination to be a more sensitive and reliable index than that of either serum amylase or serum lipase. An increased level of pancreatic desoxyribonuclease greater than five times the highest normal level has been reported in patients with hemorrhagic pancreatitis by Kowlessar and McEvoy.[7]

Other positive laboratory findings[8] may include hypocalcemia, hyperglycemia, hyperbilirubinemia, hypoprothrombinemia, positive findings on cephalin flocculation, thymol turbidity, and thymol flocculation tests, hyperlipemia, glycosuria, ketonuria, bilirubinuria, and an increased concentration of amylase in the urine.

Acute Disease—Diagnosis

The diagnosis of acute pancreatitis usually depends on the finding of a high serum amylase level in a patient with acute severe pain in the upper abdomen and tenderness, vomiting, fever, increased pulse rate, and leukocytosis.

Certain roentgenographic procedures may be helpful in the diagnosis. A survey film of the abdomen may reveal a "sentinel loop" of localized paralytic ileus, usually in the left mid-portion of the abdomen, calcification in the region of the pancreas, or the "colon cut-off" sign. The latter consists of an isolated gaseous distention of the ascending colon and hepatic flexure due to partial obstruction caused by spread of the inflammatory process from the head of the pancreas, as reported by Price in 1956. The barium meal study may disclose the "papillary sign," an unusual prominence of the papilla, as well as evidence of extrinsic pressure on the stomach, duodenal loop, or left half of the transverse colon. Occasionally, the diagnosis is difficult and, at times, impossible without resorting to laparotomy.

In the differential diagnosis, other causes of pain in the upper abdomen also require consideration. Perforated peptic ulcer is ordinarily associated with a greater degree of abdominal wall rigidity and can readily be differentiated by the demonstration of free air in the uppermost portions of the abdomen on a survey roentgenogram. Biliary colic is usually associated with tenderness in the region of the gallbladder. The patient, as a rule, does not appear as sick as does the one with acute pancreatitis. The pain of biliary colic does not last as long as that of pancreatitis, tends to spread and progress less, and may be in some cases temporarily relieved by nitroglycerin. Peritonitis due to causes other than a ruptured peptic ulcer is not usually preceded by the severe prostrating epigastric pain of acute pancreatitis. A moderately elevated serum amylase level in certain patients with peritonitis may be encountered and prove misleading if this criterion alone is used. Intestinal obstruction may be differentiated on auscultation by the high-pitched peristalsis occurring in regular periodic rushes (unless an opiate was recently administered) and on survey roentgenograms of the abdomen by the demonstration of gas-fluid levels. Occlusion of the mesenteric vessels, rupture of an aneurysm, and other causes of intra-abdominal pain may be differentiated, except under unusual circumstances, by normal serum amylase levels.

Coronary occlusion may be confusing, especially when pancreatitis is associated with shock. Acute pancreatitis has been reported to cause electrocardiographic changes[9] suggestive of myocardial infarction during the period of increased serum enzyme concentration. The changes include depression of the S-T segment, inversion of the T waves, and prolongation of the Q-T interval. They have been ascribed to a toxic substance in the blood stream arising from the pancreas, to coronary insufficiency secondary to shock and hypotension, and to the direct action of pancreatic enzymes on the structures of the heart. The electrocardiographic changes are not specific for acute pancreatitis but may be observed in a variety of conditions in which shock and electrolyte disturbances are present.

The finding of an elevated serum amylase level does not always mean that pancreatitis is responsible. The administration of opiates has been reported to be followed by a moderate elevation of serum amylase level, which may persist for as long as 24 hours. Usually the levels reached are not as high as those encountered in the early phase of acute pancreatitis. The serum amylase level may be elevated when renal function is impaired to a degree causing an elevation of blood urea nitrogen level. Sachar and Weinhaus, in 1956, reported an impaired renal clearance of pancreatic amylase which they thought was responsible for hyperamylasemia in a patient without obvious renal or pancreatic disease.

Acute Disease—Complications and Treatment

Complications.—The acute process may subside, or it may remain active until shock or sepsis terminates the picture. When death occurs within a few hours of the onset of the pain, it is usually the result of shock. The shock has been ascribed to a decreased blood volume occurring when the edema first appears.[10] When death occurs after three or more days have elapsed, it is usually the result of sepsis or severe internal hemorrhage. The peritonitis at first is chemical in nature, but, subsequently, secondary bacterial invaders appear, including gas-forming anaerobes, to cause a bacterial peritonitis, septicemia, septic thrombosis of the portal vein, or multiple abscesses. Shock may occur as a result of excessive blood loss into the peritoneal cavity due to erosion of a sizable blood vessel. Other hemorrhagic manifestations that may develop include purpura, hematemesis, melena, and extravasation of blood into the mediastinum or abdominal wall. Obstruction of the jejunum or of the colon may occur as a result of involvement by an inflammatory mass about the body and tail of the pancreas.

Diabetic coma may complicate acute pancreatitis.[11] The distinguishing characteristics of the diabetic coma in patients with acute pancreatitis have been said to be a rapid fall in blood sugar levels in response to insulin, a water-resistant dehydration that responds to the expansion of the blood volume, brief periods of increased production of insulin or reduction of glucagon, severe degree of prostration, abdominal pain of pancreatic distribution, abdominal tenderness on palpation, sweating at some stage of the disease, elevated serum amylase levels, and failure to improve despite therapy.

Treatment.—In the past, many patients with acute pancreatitis were subjected to laparotomy because of the uncertainty of making an absolute diagnosis on purely clinical evidence. The mortality was high. During recent years increased confidence in the clinical diagnosis, resulting from more widespread use of the serum enzyme tests, has led to increasingly conservative management. Because of this and the improved methods of combating shock and sepsis in critically ill patients, the mortality from severe pancreatitis has decreased. Unfortunately, a certain number of patients have died when either medical or surgical therapy was used alone, indicating that the manner of treatment must be individualized and the plan of therapy chosen which offers the best prognosis. When operation is necessary it should be carried out at an appropriate time after the onset of acute symptoms and not during the early hours, unless suppuration, severe hemorrhage, or spreading peritonitis develops.

Conservative management includes bed rest and nothing given by mouth until the acute symptoms have subsided. Continuous gastric suction is maintained through a nasogastric tube in order to remove acid gastric juice, a natural stimulant to pancreatic secretion, and to reduce ileus. Atropine, 0.4 to 0.6 mg., is given by injection every three to four hours to suppress pancreatic as well as gastric acid secretion. Meperidine is preferred to morphine for pain because of the greater tendency of the latter to cause nausea and its demonstrated ability to cause spasm of the sphincter of Oddi with a resultant increase in pressure within the pancreatic ductal system. Tetraethylammonium (Etamon) chloride, 1 to 5 ml. of a 10% solution given intravenously every four hours, has controlled pain satisfactorily in some instances. At times, intractable pain has been promptly relieved by paravertebral, epidural, or splanchnic block.

Shock is combated by infusions of plasma, albumin, or blood. Parenterally given fluid, in the form of isotonic sodium chloride solution, is administered to overcome dehydration and to replace the chloride lost by vomiting and gastric aspiration. Potassium should be administered along with sodium to patients in whom large amounts of gastric content are aspirated because large amounts of potassium may be lost in this manner. Glucose solutions should not be given when a hyperglycemia exists, unless covering amounts of insulin (5 to 10 units of regular per 25 Gm. of glucose) are given. When insulin is used, great care must be exercised to avoid a fall in the blood sugar level to hypoglycemic levels. Calcium gluconate and vitamin K are injected parenterally when the serum calcium or plasma prothrombin levels are low. A broad-spectrum antibiotic may be administered in an attempt to prevent or suppress suppurative complications. Beneficial results from the use of cortisone have been reported in several instances. Dreiling and co-workers,[12] however, feel that the use of the steroids should be limited to patients with acute pancreatitis who have adrenocortical deficiencies, because of the experimental production of pathological damage to the acinar tissue of the pancreas that has followed the administration of these compounds, as well as because of postmortem evidence that similar changes occur in patients on steroid therapy. They found a depressant effect of steroids on the external secretion of the pancreas, which they ascribed to an interference with the proper functioning of acinar tissues.

The patient is permitted to take fluid and bland foods by mouth as soon as the acute symptoms subside. Thereafter, measures to eliminate such precipitating factors as cholelithiasis, alcoholism, peptic ulcer, or hyperparathyroidism should be instituted for prophylactic purposes. It should be pointed out that a cholecystogram may reveal a nonfunctioning gallbladder if performed too soon after an attack of pancreatitis. At least a month and sometimes longer should elapse before any significance need be attached to such a finding unless confirmatory evidence of cholelithiasis is obtained by biliary drainage. A glucose tolerance test should be performed on all patients to detect latent diabetes unless a diabetic state is obvious.

Chronic Disease—Etiology and Clinical Manifestations

Etiology.—Chronic pancreatitis is encountered most frequently during the fifth and sixth decades of life. It is usually caused by repeated attacks of acute pancreatitis. It may also occur as a result of involvement by tuberculosis, syphilis, or hemochromatosis. The development of chronic pancreatitis in younger individuals on a hereditary basis has been reported by Comfort and associates. It is inherited through a non-sex-linked Mendelian dominant gene and is accompanied by a defect in amino acid metabolism, the distinctive feature of which is an excessive lysinuria.[13] It is not associated with gallstones, and alcoholism is not a factor.

Clinical Manifestations.—The clinical manifestations of chronic pancreatitis depend on the stage of the disease. During a relapse the manifestations are similar to those of acute pancreatitis. Subsequently, the clinical picture may be quite variable, depending on the degree to which the acinar and islet tissues are destroyed, the nature of the associated disease process, the presence or absence of calcification, and whether obstructive jaundice is produced. The clinical picture may also be modified by alcoholism and drug addiction, as well as the manifestations of hyperparathyroidism.

The chronic relapsing form is characterized by recurring attacks of acute and severe pain interspersed with variable intervals of relative freedom from symptoms. The painful episodes, associated with nausea, vomiting, constipation or diarrhea, fever, chills, tendency to tachycardia, and, sometimes, jaundice, may occur as infrequently as once in four years or as often as once daily or weekly; they have been known to last from less than one hour to 35 days. The pain is most frequently experienced in the epigastrium, then, in order of frequency, in the right upper quadrant, the left upper part of the abdomen, the right lower quadrant, and the periumbilical region. It may also be generalized. Radiation to the back is common. The pain, when typical, is severe and steady and tends to make the patient flex his spine forward for relief. The onset may be gradual or abrupt. Frequently, it gradually increases in severity, reaches a plateau, and then gradually declines. It may be temporarily relieved by opiates. Some patients have difficulty in describing the exact character of the pain but readily admit its marked severity.

Physical examination of the abdomen during an acute painful episode may reveal the signs of acute pancreatitis. In addition, an epigastric mass may be found, consisting of pancreas, enlarged because of inflammation or contained cysts, and, in some cases, hepatomegaly as a result of fatty infiltration. Early in the acute episode, the function of the acinar and islet cells is frequently disturbed. Eventually, the cellular disturbances become more permanent and cause steatorrhea and diabetes mellitus. Loss of weight, despite a good appetite and a satisfactory calorie intake, occurs as a result of faulty digestion and absorption of fat. The character of the stools changes, and their number increases when steatorrhea develops. The characteristic stool is bulky, frothy, glistening, pale in color, and foul-smelling. Sometimes, diabetes and/or steatorrhea first attract attention to the existence of a destructive inflammatory process in the pancreas.

Occasionally, the clinical picture is dominated by a progressive jaundice occurring as a result of compression of the common duct by the enlarged head of the pancreas. In such cases, the clinical diagnosis is usually that of carcinoma of the pancreas, and the true nature of the process is disclosed at laparotomy. In rare instances, obstruction of the colon thought to be due to a carcinoma is found to be the result of stenosis secondary to chronic pancreatitis. An instance of portal hypertension with hemorrhage from esophageal varices, secondary to recurrent pancreatitis, was reported by Snider and Nelson. They felt that the portal vein was probably compressed by the inflammatory process in the head and neck of the pancreas. The development of chronic pancreatitis without a history of acute painful episodes has been reported by Bartholomew and Comfort.

Chronic Disease—Diagnosis

Early in the course of the disease, the diagnosis is based on a history of recurring attacks of acute pancreatitis having the clinical and laboratory characteristics previously described. Subsequently, as the pancreas becomes progressively and extensively damaged, the functioning acinar cells may be too few to give an elevation of values for serum enzymes during the painful seizures and the diagnosis is based on the clinical picture, together with the laboratory findings, including hyperglycemia, glycosuria, a diabetic type of glucose tolerance curve, and a decreased volume and concentration of one or more of the pancreatic enzymes in the duodenal juice before and after the administration of a stimulant, such as secretin, bethanechol (Urecholine) chloride, or methacholine (Mecholyl). An increased amount of nitrogen and of total and unsplit fat may be detected in the feces while the patient is maintained on a diet containing fixed amounts of fat, protein, and carbohydrate. Evidence of impaired digestion and absorption of neutral fat may also be obtained by determining blood and stool concentrations of radioactive iodine (I^{131}) after feeding fat so labeled.

Roentgenographic demonstration of calcification in the region of the pancreas furnishes additional evidence of chronic pancreatitis. Such calcification, on the basis of relapsing pancreatitis, has been observed to become evident anywhere from 1 to 22 years after the onset of pain. The possibility of the existence of a parathyroid adenoma should be kept in mind in all cases of diffuse calcification of the pancreas. Other roentgenographic findings may include widening of the duodenal loop, compression or indentation of the duodenum, compression of the antrum or posterior wall of the stomach, and anterior displacement of the stomach. Disturbances in the motor function and pattern of the small intestine may be detected. Their presence depends on the blood sugar level at the time of the examination, the presence or absence of hypoproteinemia, and abnormal serum potassium and calcium levels. A cholecystogram may reveal a normally functioning or a nonfunctioning gallbladder, with or without evidence of calculi.

In the differential diagnosis of the acute painful episodes of chronic relapsing pancreatitis, the same causes of abdominal pain as were discussed in the section on acute pancreatitis are to be kept in mind. In the differential diagnosis of chronic pancreatitis associated with steatorrhea, sprue must be considered. Sprue is characterized by relapses and remissions of symptoms, consisting of anorexia, flatulence, loss of weight, passage of foul-smelling flatus and bulky stools, a flat oral glucose tolerance curve, and a lack of the laboratory abnormalities characteristic of a damaged pancreas. Intestinal lipodystrophy (Whipple's disease) may also be associated with steatorrhea as a result of deposits of fat and fatty acids in the intestinal and mesenteric lymphatic tissues. Associated clinical manifestations of intestinal lipodystrophy may include flatulence, arthritis, loss of weight, anemia, edema, ascites, cutaneous pigmentation, and evidence of a low-grade inflammatory involvement of the peritoneal, pleural, and pericardial cavities.

When obstructive jaundice is present, a differential diagnosis between chronic pancreatitis and carcinoma of the pancreas is not possible on the basis of the fat content of the stools, the glucose tolerance curve, the concentration of pancreatic enzymes in aspirated duodenal juice, or the roentgenographic demonstration of obstruction or distortion of the duodenum or stomach. The finding of malignant cells in aspirated duodenal juice or the demonstration of metastases supports a diagnosis of carcinoma. Carcinoma is more likely to be associated with anorexia, cachexia, and pain, which is usually less acutely severe but more persistent. It is intensified when the patient is lying in the supine position and relieved by forward flexion of the spine as in the fetal or knee-chest positions. Occasionally, at laparotomy, a biopsy of the pancreas will reveal extensive fibrosis and chronic inflammation secondary to an undetected carcinoma of the pancreas. The inflammatory reaction is secondary to the malignancy. Bartholomew and associates have noted the development of carcinoma of the pancreas in patients with long-standing pancreatitis associated with calcification. In Senior's [14] series of 96 patients collected at the University Hospital and thought to have chronic pancreatitis, 12 eventually were discovered to have carcinoma of the pancreas. Exploration and biopsy of the pancreas had been done in some of the 12, the biopsy disclosing only evidence of chronic pancreatitis.

The problem is a difficult one, and differentiation is not always possible clinically, grossly at laparotomy, or even on biopsy. Some patients with chronic relapsing pancreatitis have had their symptoms ascribed to psychoneurosis. One must always bear in mind that the clinical picture may be confused by alcoholism or drug addiction.

Chronic Disease—Course, Prognosis, and Treatment

Course and Prognosis.—The course of chronic relapsing pancreatitis depends to a large extent on the maintenance and persistence of the etiological factors and on the degree to which the pancreas is damaged. Eventually, the state of chronic pancreatitis is reached, with varying degrees of pancreatic insufficiency as manifested by diabetes, steatorrhea, and calcification. Death may occur at any time from intercurrent infection, pancreatic necrosis, peritonitis, abscess, septicemia, pyelophlebitis, complications of diabetes, intra-abdominal bleeding, or gastrointestinal hemorrhage from peptic ulcer or gastroduodenitis.

Medical management in the presence of severe pain is unsatisfactory and is often complicated by drug addiction and alcoholism. A variety of surgical procedures has been employed, with results sometimes satisfactory but often as unpredictable as those of medical therapy.

Treatment.—Chronic relapsing pancreatitis may be treated medically, surgically, or by a combination of these methods.

Medical treatment is purely palliative and consists of relief of pain, substitution therapy in patients with pancreatic insufficiency, and eradication of etiological factors of a nonsurgical nature. The treatment of the painful attack is similar to that of acute pancreatitis. In the intervals between attacks, and especially when pancreatic insufficiency develops, the diet should be high in carbohydrate and readily assimilable protein but low in fat. If gastric hyperacidity exists, gastric secretory depressant drugs should be administered in an attempt to prevent peptic ulceration of the duodenum, to which such patients are predisposed when the amount of bicarbonate eliminated by the diseased pancreas becomes decreased. The administration of predigested protein in supplemental feedings may aid in maintaining a positive nitrogen balance. An active form of pancreatin is administered in sufficient amounts (up to 3 Gm. with each meal) to decrease steatorrhea and azotorrhea as well as a multivitamin capsule daily to insure an adequate intake of the essential vitamins. Bile salt preparations may be administered to increase the absorption of fat-soluble vitamins, especially in patients with jaundice, as in these the bile salt concentration may be decreased. Choline or methionine are indicated for those patients whose protein intake is inadequate in an attempt to prevent subsequent development of a fatty liver and possible cirrhosis. Diabetes should be controlled with insulin. The use of alcoholic beverages should be discontinued by those in whom alcoholism appears to be the major precipitating factor. Gastroduodenal disease, when present, should be properly treated.

Jaundice due to obstruction of the common bile duct by an enlarged head of the pancreas requires a surgical procedure, such as a cholecystenterostomy. Cholelithiasis and choledocholithiasis should be treated surgically in an attempt to relieve those patients in whom biliary tract disease may be the predisposing factor. For repeated attacks of severe pain, not controlled by conservative measures, a variety of surgical procedures has been employed.

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PROGRAM ON MEDICAL ASPECTS OF AUTOMOBILE INJURIES AND DEATHS

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The American Medical Association, appalled by the rising tide of deaths and injuries occasioned by the automobile and realizing that a certain undetermined percentage were due to physiological conditions, pathological states, emotional disturbances, or drugs and alcohol, appointed a committee, through its Board of Trustees, to study and report on the medical aspects of automobile crash injuries and deaths in 1955. This committee was to determine the magnitude of the problem, study the epidemiology and methods of prevention and cure primarily from a purely medical standpoint, and determine the role of the physician in obtaining these objectives.

The first endeavor of the committee was to acquaint the medical profession with these broad aspects by presenting a symposium at the 1956 meeting in Chicago. At the same time a rather comprehensive scientific exhibit was also presented. This effort was well received and many requests for reprints were received from both American and foreign physicians. A 15-minute movie called "On Impact" was also prepared in collaboration with the Ford Motor Company. This film depicted some of our efforts toward curbing this rising tide of injuries.

The committee decided that its first duty was to prepare three pamphlets. The first one has been written at the popular level in lay language to serve as a guide to the patient in answer to the query "Are you fit to drive?" The first 100,000 copies were paid for by the Association of Casualty and

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Clinical Professor of Otolaryngology, University of Virginia, Department of Medicine. Chairman, American Medical Association Committee on Medical Aspects of Automobile Injuries and Deaths.

Read in the Session on Traffic Accidents before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Surety Companies of New York. The Center for Safety Education of New York University collaborated in this venture.

The second pamphlet is designed to serve as a guide to the physician in determining a patient's fitness to drive. This is a pioneer work; it has been completed and will be published in a future issue of THE JOURNAL. The material will be presented under such sections as cardiovascular and ophthalmological aspects. The third and most comprehensive pamphlet will be written as a guide to examining police officers and state traffic agencies and will set certain physical standards. We have also suggested that each state medical society appoint a traffic safety committee to work with various state agencies.

Our studies over the past two years have shown that there are many divergent medical interests in many phases of this problem. For instance, we are working through the National Safety Council in establishing uniform and reasonable speed limits. We are collaborating with the American College of Surgeons for safer automobile design. We are working through the Roberts' Congressional Committee to this same end and to assist in providing new and needed legislation. We have given our conclusions in regard to alcohol blood levels to the legal division of the A. M. A. and to the Committee on Alcohol. Finally, we hope to establish a set of uniform objectives that will guide us and the various state and local safety committees.

400 Locust Ave.

MEDICAL GUIDE FOR PHYSICIANS IN DETERMINING FITNESS TO DRIVE A MOTOR VEHICLE

Seward E. Miller, M.D., Ann Arbor, Mich.
and
Harold Brandaleone, M.D., New York

Traffic accidents killed about 40,000 individuals last year and injured about 1,500,000. This constitutes one of the nation's largest unsolved health hazards. Physicians have not realized or accepted their responsibilities in this health problem as they have with heart disease, cancer, and other disease entities.

Since the human factor is the most important single factor responsible for motor vehicle accidents, the physician must initiate and participate in research designed to determine the relationship between physical and emotional factors and the etiology of accidents. He is the only person able to ascertain the physical, mental, emotional, or physiological impairments of an individual and to evaluate these disabilities in relation to safe driving ability. It is the responsibility of the physician to persuade a patient to discontinue driving when he no longer is able to drive with safety.

Motor vehicle drivers may be classified as two general types: civilian or private drivers and commercial or industrial drivers. The latter group includes transportation drivers. The required physical and mental standards for commercial vehicle drivers, especially transportation drivers, should be more rigid than for civilian drivers. The civilian driver should be examined every three years up to the age of 45 years and every two years thereafter. The commercial vehicle driver should have a preplacement examination and a periodic examination every two years up to the age of 45 years and annually thereafter.

A patient may incur temporary or permanent disability which should prevent him from driving. He may be suffering with an illness that directly or indirectly interferes with his driving ability, making it unsafe for him to drive until the condition is controlled. For example, everyone agrees that a diabetic who takes insulin and is subject to hypoglycemic reactions should not drive, nor should a patient with uncontrolled convulsions or a cardiac condition that might cause sudden loss of consciousness.

The Committee on Medical Aspects of Automobile Injuries and Deaths has prepared a medical guide for physicians in determining fitness to drive a motor vehicle which will be useful in advising patients on their fitness to drive. The guide will be published in a future issue of THE JOURNAL.

1634 University Hospital (Dr. Miller).

Read in the Session on Traffic Accidents before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

ROLE OF PRIVATE PHYSICIAN IN MOTOR VEHICLE ACCIDENT PREVENTION

James L. Goddard, M.D., M.P.H., Washington, D. C.

The physician can help in at least five ways to reduce the damage done to human lives by motor vehicle accidents. He can "teach while treating" by explaining the relation of defects and diseases to accidents. He can and should make sure that community emergency services are improved. He can make sure that emergency rooms in hospitals are organized in such a way that a sudden influx of accident victims will not create chaos. He can influence the development of sound medical standards for driver licensing. He can engage in research on the causes and prevention of accidents. The fact that more than 4 million persons require physicians' services because of motor vehicle accidents represents at once a responsibility and an opportunity in the field of preventive medicine.

The practicing physician has long been concerned with the problems generated by motor vehicle accidents, primarily, the provision of medical services to the injured. The true magnitude of his task has only come to light in the past year. The recent report of the National Health Survey indicates that 2,500,000 persons were injured in motor vehicle accidents from July 1 to Dec. 31, 1957. Approximately 85% of those injured required medical attention. This means that each year over 4 million persons require physicians' services because of motor vehicle accidents.

It is, therefore, not surprising that physicians are now looking beyond the immediate task of restoring accident victims and asking that more resources be devoted to the prevention of accidents and resultant injuries. Individually and collectively, physicians have expressed their concern with the injury-producing potential of the automobile. Through the American Medical Association and other medical organizations, this concern has been voiced by asking that more attention be given to the design of vehicles which will minimize the danger of injury, should an accident occur.

Through improvements in clinical knowledge, methods, and skill, physicians have helped to hold the total number of fatalities at a rather fixed level. No precise measure of this contribution can be made, but it is known that fatalities have remained constant in spite of a tremendous increase over the past 20 years in the total miles traveled annually.

Two years ago the Committee on Medical Aspects of Automobile Injuries and Deaths, of the American Medical Association, was organized in order to utilize more effectively the interests and resources of the medical profession towards the solution of this complex problem. As indicated by its name, the committee has restricted its efforts to a particular segment of the problem. The committee recognizes that, to be successful, physicians must not dissipate their interests and energies by going into aspects of the problem in which they are not competent. The physicians must examine their capabilities and accept responsibility for suitable activities.

The following activities are proposed as meeting the above criteria. If implemented by every physician, they would result in significant decreases in deaths, injuries, and disabilities. First, there are the many things that can be done as a physician, working with patients. The traditional physician-patient relationship provides the ideal situation for patient guidance in accident prevention.

One thinks immediately of the obvious opportunity which occurs when the physician is actually treating an injury and can "teach while treating," by explaining accident causation and warning against potential future hazards. I use the term "ideal" because no learning situation could be better calculated to produce attention and acceptance on the part of the patient.

Beyond this special situation, however, additional guidance possibilities are almost limitless. When the physician, in the course of his normal practice, discusses with patients conditions or disabilities that could interfere with the ability to drive a motor car, there should be frank counseling on this subject, and the hazards of driving should be plainly indicated. Possible relationship of side-effects of medication on driving ability should be stressed.

In addition, inadequate vision and hearing, diabetes, epilepsy, and heart and neuromuscular conditions (to name but a few) can create serious driving hazards. The physician's advice in this connection will carry weight with the patient, while the latter may not otherwise give proper emphasis to the relationship between his condition and his driving capacity.

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Read in the Session on Traffic Accidents before the Section on Miscellaneous Topics at the 107th Annual Meeting of the American Medical Association, San Francisco, June 25, 1958.

Emergency Services

The second major responsibility of the medical profession is to improve community emergency services. The care and transport of the injured is a matter that has not received the attention it deserves. Studies made during World War II and the Korean war demonstrated the great values of properly administered first aid and careful handling during transport to the medical facility. Implicit in good community emergency services, whether provided by public or private organizations, are the following standards: (1) trained drivers and attendants for all ambulances, (2) continued supervision of emergency services, and (3) adequacy of equipment.

There are several ways of achieving these objectives. In some areas full-time rescue squads are in existence. The physician, through his local medical society, can provide the training that is indicated. Where a community relies on private services it has proved feasible, in some areas, to require training of drivers and attendants as a prerequisite to licensing. In some communities the local health department is the licensing and supervisory agency. But in each instance the best interest of the patient is served when the physicians of the community are active in the training and continued supervision of the services.

Third, and equally important in any community, is the status of the hospital emergency services. A direct contribution can be made here if physicians will exert themselves to improve and coordinate the services in hospital emergency rooms. The team approach is all important in rendering these services, which have so great an influence on minimizing the effects of accidental injury, and much remains to be done to raise the standards of hospital emergency rooms throughout the country.

Specifically, the emergency rooms should be organized in such a way that a sudden influx of accident victims will not create chaos. This means better planning and supervision on the part of the attending staff. This important phase of patient care cannot be delegated to the intern and resident staff. Ancillary services, such as x-ray and laboratory, should be available either immediately or within a few minutes, and the equipment must be adequate.

These three activities, patient guidance, improvement in community emergency services, and improvements in hospital care, require the support and participation of physicians individually and at the community level.

Other Contributions by Physicians

Working through the State Medical Society, the practicing physician can make a fourth major contribution. I refer to the development of sound medical standards for driver licensing. This can be achieved by providing the motor vehicle administrator with a technically competent advisory group. This advisory group can also provide guidance to the motor vehicle administrator in the handling of problem cases. In some states the Medical Society and the State Health Department have worked jointly with the licensing authority to establish special procedures for the supervision of drivers thought to represent added risks, e. g., epileptic.

The importance of a physician's role in research hardly needs emphasis. Through such cooperative endeavors as the Cornell Automotive Crash Injury Research Project, he has made a significant contribution. It is not unreasonable to expect an increased interest in accident prevention research. By virtue of his access to the clinical data and his training, the physician is particularly well qualified to carry out such investigations.

Thus the physician, as a physician, can make five contributions: (1) give individual patient guidance, (2) improve community emergency services, (3) improve hospital emergency services, (4) develop medical standards for drivers' licensing, and (5) engage in auto accident research.

In addition, as a leading member of the community, the physician can make a significant contribution to accident prevention by lending his support to every worthwhile local effort to cut the accident rate. For example, driver education, organized at the high school level, has demonstrably improved teenage driving habits, and equally gratifying results can be anticipated from adult driver education. The encouragement and development of adequate driver training programs in a community require organized community effort; physicians, acting either individually or as medical society members, can exert leadership in this important area. The physician's word will also carry weight in any community when he supports movements for improved enforcement of traffic laws.

Public health officials throughout the United States are laying special emphasis on better first-aid training. Here the physician is the indispensable person. The physician can help by emphasizing the need for first-aid training and its benefits, and by counseling the instructors. Although my topic has been the physician's role in accident prevention, the cooperative relationship between the private physician and the public health profession in this vital field of activity should also be mentioned. The stimulation and guidance of community action to reduce the terrific toll of death and disability from accidents in this country is an important responsibility of the State and local health departments, aided by the Public Health Service.

Through professional education and education of the general public, it is hoped that a significant contribution to accident prevention can be made in the years ahead. Local education campaigns of this nature can succeed only with the enthusiastic support of appropriate local groups, and no community group is a more necessary partner in this undertaking than the private physicians.

330 Independence Ave. S. W. (25).

PSYCHOLOGICAL AND PSYCHOPHYSIOLOGICAL FACTORS IN MOTOR VEHICLE ACCIDENTS

FOLLOW-UP STUDY

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A continued and more intensive investigation of the personal factors that might make some drivers more susceptible than others to automobile accidents was carried out in 20 airmen. Ten had been held officially responsible for two or more accidents in the preceding four and one-half years. They were compared with 10 who had no record of accidents in the same period. The tests included a structured psychiatric interview and a routine psychological examination as well as other functional tests. No differences were found between the two groups in either intelligence or psychophysiological responsivity. However, in the area of personality functioning, accident-repeaters displayed significantly poorer control of hostility, lower tension-tolerance, higher separation anxiety and dependency needs, and extremes both of egocentricity or sociocentricity and fantasy-preoccupation or unreflectiveness.

It has long been recognized that motor vehicle accidents are not, as the term implies, simply a function of what "erring men call chance." It has been demonstrated, for example, that some roads are safer than others and that certain times of the day are safer. There is also some evidence to indicate that certain people are more likely to have accidents than others, and a number of attempts have been made to determine whether such persons possess unique personal characteristics which differentiate them from their fellowmen who do not have accidents.

For example, in various studies the accident-repeater and nonaccident drivers have been compared on a wide variety of psychophysical and psychophysiological measures, on measures of personality structure and functioning, and on social history variables. Many of these studies have yielded equivocal or contradictory results, probably partly because of real differences between the populations studied, but probably also in many cases because of methodological deficiencies in the design of the studies—including failure to control for variations in accident exposure, unreliability in the accident criteria employed, and lack of objectivity in the measurement of driver characteristics.

The weight of the evidence, however, suggests that in most populations accident repeaters are likely to differ from other drivers in their personal characteristics and, further, that psychological variables are more likely to prove discriminating than measures of physiological or psychophysical functioning.[1]

The purpose of the present paper is to describe the most recent findings in a four-year investigation of the role of personal and interpersonal factors in determining accident frequency and severity among airmen stationed at Lowry Air Force Base in Denver. In previous work on this project, 264 subjects were administered a wide variety of psychiatric and psychological techniques, including structured psychiatric interviews, objective and projective personality tests, attitude and interest tests, and a number of psychophysical measures.

As reported previously,[2] most of these measures failed to discriminate consistently with repeated samples between high-accident, middle-accident, and nonaccident rate airmen. For example, while a number of psychophysical measures, such as discrimination reaction time and depth perception, and a number of objective personality tests, such as the Minnesota multiphasic personality inventory and the Thurstone temperament scale, appeared promising initially, they failed to survive in cross-validation. One type of measure, however, proved extremely stable, namely, measures of the individual's value system.

Of the six scales contained in a modification of the Allport-Vernon-Lindzey study of values, developed by Dr. Jerome Levy of the project staff, three scales—those dealing with esthetic, theoretical, and religious concerns—proved highly discriminating, both initially and in later cross-validation samples. The remaining scales (economic, political, and social) did not. The accident subjects were consistently less oriented toward religious values, and

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more toward esthetic and theoretical values than the nonaccident subjects. As might be expected, the mean scores of the middle-accident subjects fell in the middle range between the high-accident and nonaccident subjects.

On the basis of the scores on this test, it was possible to differentiate successfully between high-accident and nonaccident subjects in approximately 73% of cases in repeated samples over several years. While this degree of predictive success was encouraging, the authors felt that not enough was yet known of the personality structure and functioning of these subjects to interpret the psychological meaning of these test findings with confidence.

The primary aim of the present study, therefore, was to obtain a broader understanding of the characteristics of these two groups. The subjects were 10 high-accident and 10 nonaccident rate airmen, selected to be representative of the over-all accident and nonaccident populations. Each of these subjects was studied intensively. High-accident subjects were defined, as in the previous study, as individuals who had two or more accidents for which they were officially held responsible in the past four and one-half years, at least one of which occurred within the year immediately preceding testing. Nonaccident subjects were defined as individuals who had no record of accidents, according to either official records or the individual's subjective report, during the past four and one-half years. Data obtained fell into two general categories: clinical studies and objective testing.

Clinical Studies

The major portion of the present study involved an intensive clinical evaluation of 10 high-accident and 10 nonaccident rate subjects. Each subject received a structured psychiatric interview aimed at obtaining information regarding his social history and personality development as well as his current attitudes, interests, behavior, and personality functioning. This interview was tape-recorded for future reference.

In addition, each subject received a routine psychological examination by one of the clinical psychologists on the staff of the University of Colorado Medical School. The following battery was administered at one sitting: the thematic apperception test (10 cards), the Rorschach test, the Wechsler-Bellevue intelligence scale (four subtests), and the Sacks sentence completion test. In each case, the psychologist was asked to prepare a general evaluation of the subject, noting such things as over-all assets and liabilities, basic character traits, and defense mechanisms employed. In view of the intention of the investigators to avoid as much as possible influencing the specific content of the reports, no further instructions were given.

The interviews were conducted by two project members, a psychiatrist and a psychologist; the psychological testing was done by five clinical psychologists. Assignment of interviewers and testers to subjects was done randomly, and in neither case did the examiner have any knowledge of the subject's accident status.

Thus, the basic data employed in this phase of the study consisted of (1) psychiatric interview transcripts and (2) test protocols and individual psychological reports. These data were then rated independently for 13 variables hypothesized to be significantly related to accident frequency and severity on the basis of previous work. In addition, two over-all personality-type descriptions were presented, one hypothesized to represent a composite accident individual and the other a composite nonaccident individual. Raters were asked to rate subjects as more like one or the other of these two personality types.

In the case of the interview, two judges were employed—the original interviewer and the alternate interviewer. Similarly, in the case of the psychological reports and original test protocols (which were rated as a composite unit), two judges were also employed—the original tester and one of the other testers. Preliminary analysis showed a high degree of agreement between raters. In view of this evidence of reliability, the average rating of the judges was employed in all cases. The 13 variables rated by the judges included the following criteria.

Variables

1. *Amount of Underlying Hostility.*—Ratings of hostility (whether expressed or not, and regardless of how expressed) were made along a continuum from negligible to excessive. This variable was included because it has frequently been mentioned in the literature as distinguishing accident from nonaccident subjects. It was the investigators' opinion, however, that this variable was not directly related to accident susceptibility. Rather, it was felt that the importance of underlying hostility as a factor in accident susceptibility could be evaluated only in relation to the individual's capacity for control. This hypothesis led to inclusion of the next two variables.

2. *Strength of Destructive, Hostile Impulses Directed Toward Environment in Relation to Ability to Control These Impulses.*—Possible ratings of hostile impulses to environment ranged all the way from "hostility moderately or much greater than control" to "excessively greater control in relation to amount of hostility." It was predicted that accident subjects would show relatively less capacity for control in relation to strength of hostility.

3. *Aggression and Behavior.*—Raters of aggression and behavior were asked to judge which of the following descriptions most nearly character-

ized the subject: (*a*) Consistently, openly belligerent; (*b*) usually controlled but occasional outbursts of belligerence; (*c*) covertly hostile (passive-aggressive, critical, carping, indirectly aggressive toward others); (*d*) realistic, flexible, appropriately assertive; (*e*) passive, unassertive (fear of retaliation for expression of aggression); (*f*) unassertive, low drive, low energy; (*g*) depressed; and (*h*) other, to be briefly described. It was predicted that accident subjects would be more likely to fall in categories *a* through *c*, nonaccident subjects into categories *d* through *g* (only one subject fell in category *h*, about which there was no prediction).

4. *Reality Orientation.*—Possible ratings of reality orientation (realistic appraisal of own motives and environmental forces affecting subject—extent to which behavior is directed toward meeting subject's own enlightened self-interest) ranged from very poor (definite breakdown, at least occasionally in reality-testing) to excellent. It was predicted that nonaccident subjects as a group would tend to show more adequate reality orientation.

5. *Egocentric Versus Sociocentric.*—Ratings ranged from very egocentric (very self-centered, little interest in rights of others or respect for their feelings) through a neutral mid-point (neither markedly egocentric nor sociocentric, fairly good balance between satisfying own needs and respect for needs and feelings of others) to very sociocentric ("overdetermined" awareness of, interest in, and respect for rights and feelings of others). It was predicted that accident subjects would be more likely to cluster at the extremes of the continuum, with nonaccident subjects tending to fall around the midpoint.

6. *Conventionality.*—Conventionality ratings were based on the extent to which the individual was conventional in his conscious thinking, values, interests, and impulses to action, as possibly distinguished from, for example, underlying unconscious needs, or overt behavior in certain life situations. Degree of conventionality or unconventionality should not be confused with degree of over-all adjustment, which was rated separately. Possible ratings ranged from highly conventional to highly unconventional. It was predicted that accident subjects would be rated as less conventional than nonaccident subjects.

7. *Over-all Adjustment.*—The degree of over-all adjustment—ability to live happily and function effectively—was rated by satisfactory resolution of subject's needs in relation to environmental and superego demands. This should be separate from conventionality or unconventionality of this adjustment. Possible ratings ranged from definitely disturbed to excellent adjustment. It was predicted that accident subjects as a group would tend to have a somewhat poorer adjustment than nonaccident subjects.

8. *Castration Anxiety.*—Possible ratings of specific evidence of castration anxiety, or generalized fear of injury to self, ranged from high to low, with a separate category entitled "Not clearly observable in these data." This variable was included largely because it appeared prominent in many of the psychological test reports. It was predicted, though without too much confidence, that nonaccident subjects would score higher on castration anxiety than accident subjects, the rationale being that high castration anxiety might make the subject more conscious of risk and less willing to engage in risk-taking behavior.

9. *Separation Anxiety.*—Possible ratings for separation anxiety (fear of loss of love and support, concern with oral supplies) ranged from high to low, with a separate category entitled "Not clearly observable in these data." As in the case of castration anxiety, this variable was included largely because it appeared prominently in many of the psychological test reports. It was predicted, again without too much confidence, that accident subjects would score higher on separation anxiety than nonaccident subjects, the rationale being that underlying feelings of lack of love lead to resentment which might tend to be acted out against figures perceived as depriving.

10. *Extent of Fantasy Preoccupation.*—Possible ratings ranged from excessive preoccupation with fantasy satisfactions through a mid-point of "effective integration of fantasy and action, planfulness" to extremely "stimulus-bound" (likely to act directly in response to people or objects with little fantasy or reflection). It was predicted that accident subjects would tend to cluster at the extremes, while nonaccident subjects would tend to fall around the midpoint.

11. *Character Type.*—Raters were asked to judge which of a number of character types most nearly described the subject (if more than one category was used, probable priority was indicated by using numbers 1, 2, etc.—see table 2). While it was not felt that this variable was likely to prove discriminating, it was included because of the attention it has received in the literature.

12. *Ability to Tolerate Various Tensions.*—Possible ratings of tolerance to tensions (i. e. without discharging them immediately) ranged from high to low, with a separate category entitled "Not clearly observable in these data." It was predicted that high-accident subjects would reveal a lower capacity for tension tolerance.

13. *Friendship Patterns.*—Finally, raters were asked to judge which of the following categories, in their opinion, most nearly described the status of the subject's social relationships: (*a*) no close friends, few casual friends; (*b*) some close friends, few casual friends; (*c*) some close friends, many casual friends; (*d*) no close friends, many casual friends. It

was predicted that nonaccident subjects would be more likely to fall into categories *b* or *c*, with accident subjects falling primarily in categories *a* or *d*.

Composite Individuals

In addition to the above variables, raters were presented with the following two personality-type descriptions, intended to characterize hypothetical composite nonaccident (type x) and accident (type y) subjects, and were asked to state which of the two types the subject most nearly resembled.

Type X.—The type x sort of person tends to be rather conventional in his values, attitudes, and behavior. In general, he seems to gain satisfaction for his needs from his everyday life and to have a fairly clear notion of the goals he wants to attain in life and of how to pursue them. He tends generally to have respect for the rights and opinions of other people, and in turn to be pretty well accepted by others. While he may be normally assertive in defending his own rights, he is seldom extremely demanding, domineering, or combative. In some cases, he may actually be somewhat less assertive than an adequate defense of his own rights would require. Such underlying hostility as he may have tends to be pretty well controlled and is seldom expressed in an obvious "acting-out" fashion. If psychopathology is present in this type, it is most likely to take the forms of denial, overly strong needs for conformity, castration anxiety and fear of aggression from others, and overly strong needs to please or placate others.

TABLE 1.—*Ratings of Clinical Psychological Reports for Accident-Repeater and Nonaccident Groups*

	Direction		Level of Significance (if Below 0.10)
Variable, No.	Accident	Nonaccident	
2 Hostility/control ratio	Less control	More control	0.02
3 Aggression and behavior	Aggressive	Adaptive, unassertive	0.05
5 Egocentric—balanced—sociocentric	Extremes	Balanced	0.01
9 Separation anxiety	High	Low	0.01
10 Fantasy—integration—stimulus-bound	Extremes	Integration	0.10
12 Tension tolerance	Low	High	0.01*
14 General personality	Type Y	Type X	0.10

* From psychiatric interview; all others from psychological reports.

Type Y.—While there may be a fair amount of individual variation on specific characteristics, in general the type y person tends to be rather unconventional in his opinions and values and sometimes in his overt behavior. He is inclined to be rather self-oriented, to have difficulty in relating easily and warmly to other people, and to be somewhat unaware of, or insensitive to their rights and feelings. He may in some cases feel that other people are difficult to understand. He often has feelings of dissatisfaction about his everyday life and is likely not to have clearly defined goals in life or consistent, practical methods for attaining such goals as he does have. He is apt to have difficulty in controlling his hostility, which may often be excessive, and consequently may at times be inclined toward overdetermined "acting-out" behavior, either at the level of overt physical belligerence or at the level of verbal aggression—in the form of sarcasm, carping complaints, or destructive comments. He is likely at times to exercise poor judgment in his evaluation of his environment or in choosing courses of action. In some cases, he may appear overly preoccupied with his own fantasy world and relatively cut-off from social relationships with others. If psychopathology exists in this type of individual, it appears most likely to take the forms of impulsive, hostilely-toned, acting-out behavior, poor reality testing, emotional lability, impaired intellectual functioning, a highly personalized, idiosyncratic fantasy, withdrawal from interpersonal relationships, or excessive immaturity.

Results

As may be seen from table 1, 6 of the 13 variables proved discriminating between high-accident and nonaccident subjects at the 0.10 level of confidence or better and 4 proved significant below the 0.02 level (i. e. less than 2 chances in 100 that differences this large or larger could have occurred by chance). Of the 11 variables hypothesized as possibly discriminating, 6 showed significant differences in the predicted direction, either in the psychological test battery, the psychiatric interview, or both.

In comparison with nonaccident subjects, the accident subjects showed a statistically significant tendency (1) to have less capacity for managing or controlling hostility; (2) to be either excessively self-centered and indifferent to the rights of others or excessively sociocentric (i. e. characterized by an "overdetermined" awareness of, interest in, and respect for the rights and feelings of others); (3) to be either excessively preoccupied with fantasy satisfactions or extremely "stimulus-bound"; (4) to be more fearful of loss of love and support (and, by inference, more angry and resentful toward persons viewed as depriving); and (5) to be generally less able to tolerate tension without discharging it immediately. In addition, the accident subjects tended to be categorized more frequently as consistently or occasionally belligerent or covertly hostile, and less frequently as only appropriately assertive, or unassertive. While not statistically significant, there were tendencies for the accident subjects to be rated as more conventional and generally better adjusted. There were no differences between accident and nonaccident subjects in ratings of reality orientation, castration anxiety, or friendship patterns.

Of the two variables hypothesized not to be discriminating, neither showed significant differences. Neither hostility alone, without reference to capacity for control, nor clinical character type showed any clear-cut trends. The distribution of accident and nonaccident subjects among the various character types is shown in table 2. Only subjects on whom both psychological test raters independently agreed are included in this comparison. Agreement was shown in 18 cases and disagreement in 2 cases. As may be seen, both accident and nonaccident subjects are distributed across a large number of categories, and there is little tendency for either accident or nonaccident subjects to concentrate in any particular category or categories. While the number of subjects in this study is too small to refute the hypothesis that certain clinical character types are more frequent among accident than nonaccident subjects, it seems clear that no single category could account for a majority of either accident or nonaccident subjects.

It will be noted that the predictive success of the clinical testing was considerably greater than that of the psychiatric interviews. While this fact may well reflect real differences in the predictive potential of the two measures, it should be pointed out that electronic recording difficulties resulted in incompleteness in a number of the interview transcripts, and this may well have lowered the predictive value of this measure.

It should also be observed that the present findings have not been cross-validated on other samples of subjects. This should certainly be done before the present results can be accepted without reservation. It may be that one or more of these findings will eventually prove to be the result of chance. However, it appears extremely unlikely that cross-validation will fail to support the main body of the findings, since it is extremely unlikely that significant differences would be obtained in 6 out of 11 cases by chance, especially with relatively small sample sizes.

The ratings of the two over-all personality-type descriptions resulted in correct discrimination of both accident and nonaccident subjects in 70% of the cases. Despite the small number of subjects, such a result would be expected by chance less than 10 times in 100. Thus, while a number of the specific variables rated had somewhat greater predictive value, in general it would appear that these personality-type descriptions provide a fairly adequate picture of the hypothetical composite accident and nonaccident individuals.

Objective Testing

In addition to the clinical studies described above, all subjects were administered a number of objective measures of interest, intelligence, psychophysical skills, and psychophysiological functioning. (Several of these measures, such as the Wechsler-Bellevue intelligence scale, were actually administered as part of the clinical studies, and analyzed clinically at that time, but the results of formal scoring will be considered here simply for expositional convenience.) Each of these measures will be discussed briefly, together with the results obtained.

The modified Allport-Vernon-Lindzey study of values measure, which had repeatedly proved discriminating in previous work on this project, was again administered. With use of the same formula (based on a combination of religious, theoretical, and esthetic scale scores) as in previous samples, 70% of subjects in the present group were correctly identified as accident or nonaccident type. This figure is significant at the 0.05 level of confidence and compares with discriminations of 73% in three previous samples.[2]

The Kuder preference record is basically a vocational interest test which yields measures of the extent of the individual's interest along 10 dimensions (outdoor, mechanical, computational, scientific, persuasive, artistic, literary, musical, social service, and clerical). The Kuder test was included in the present battery because previous results with the study of values suggested that other interest measures might also prove discriminating. As it turned out, most of the scales did not prove discriminating. However, a formula based on the computational and scientific scales (on which accident subjects were high) and the persuasive and clerical scales (on which nonaccident subjects were high), made it possible to identify 81% of subjects correctly as accident or nonaccident type. While this figure is significant at the 0.02 level, it cannot be accepted confidently until it has been cross-validated.

TABLE 2.—*Distribution of Character Type Ratings Among Accident-Repeater and Nonaccident Subjects*

	A*	N*		A	N
1 Hysteroid	0	1	8. Neurasthenic	0	0
2. Phobic	1	0	9. Paranoid	0	0
3. Obsessive	0	2	10. Psychopathic	1	0
4. Compulsive	1	0	11. Passive aggressive	2	2
5. Cycloid	0	0	12. Passive dependent	1	1
6. Schizoid	1	3	13. Aggressive reaction	1	0
7. Anxiety state	0	0	14. Intellect disorder	1	0

* A = accident repeater; N = nonaccident.

The American transit motor abilities test, developed by Kraft and his associates [3] in their studies of bus drivers, is intended as a measure of driving aptitude. The subject is seated at the wheel of a mock-up bus and, in response to visual light patterns on a board across the room, is required to carry out various maneuvers with brake, steering wheel, gearshift, and clutch. All responses are recorded electrically. In this situation, accident subjects reacted more quickly and took less time to complete the task but made more errors than nonaccident subjects. All measures were significant at the 0.05 level of confidence or better.

All subjects were examined for psychophysiological responsiveness, under both resting and stress conditions (i. e., before, during, and after presentation of an incomplete sentences test containing both emotionally charged and neutral topics). The scores obtained included measures of respiration, muscle tension, psychogalvanic skin reflex, heart rate, and a combined measure of over-all reactivity. While wide individual differences occurred among subjects in their psychophysiological responsiveness on all measures, none of the measures proved discriminating between accident and nonaccident subjects, although there was some tendency for the accident group to have a slightly faster heart rate during presentation of the test.

TABLE 3.—*Intelligence Test Scores of Accident-Repeater and Nonaccident Groups*

	Means	
	A*	N*
1. Wechsler adult intelligence scale		
Prorated intelligence quotient	105.3	106.3
Weighted subtest scores		
Information	10.6	10.2
Comprehension	11.9	12.0
Similarities	10.6	11.4
Block design	11.4	11.9
2. Shipley-Hartford vocabulary score	27.8	25.9

* A = accident-repeater; N = nonaccident.

All subjects were administered two measures of intelligence, a portion of the Wechsler-Bellevue adult intelligence scale (four subtests), and the Shipley-Hartford vocabulary scale. As may be seen from table 3, no significant differences between the accident and nonaccident subjects were obtained on any of these measures. Thus, it would appear that the differences between accident and nonaccident groups which were found on other measures could not be attributed to differences in the over-all intellectual level of the two groups.

In previous phases of this research,[2] subjects were administered the Minnesota multiphasic personality inventory (MMPI) and a social history questionnaire. While neither of these measures as a whole proved helpful, item analysis yielded a number of items which in themselves appeared promising but which required cross-validation before they could be confidently accepted. For this reason, these items were repeated with the present sample of subjects. These items and their level of significance in the 1955 and 1956 samples, as well as in the current study, are shown in table 4. As may be seen, very few of these items continue to prove discriminating with repeated testing. The overwhelmingly negative character of these findings, particularly on the MMPI, appears especially interesting, since these findings conflict with those of other investigators on somewhat similar samples of subjects.[4]

The Rorschach and the thematic apperception test (TAT), which had been individually administered to each subject during the clinical phase of this study and interpreted clinically at that time, were later scored objectively for a number of differentiating characteristics derived from previous samples.[2] The accident and nonaccident groups were compared across scores for these characteristics. On both the Rorschach and TAT scores, the differences between the accident and nonaccident groups were not sufficiently pronounced to meet the 0.10 level of statistical significance required.

Comment

While previous research on the present project demonstrated that the accident-repeater and nonaccident airmen differed significantly from one another, and while certain isolated psychological measures proved highly predictive of accident status for this population, the psychological significance of these measures was difficult to interpret. It was felt that further research was necessary before a clearer understanding of the psychodynamic relationships existing between the structure and functioning of the individual and his accident susceptibility could be achieved.

The primary aim of the present study, therefore, was to obtain a broader knowledge of the characteristics of accident and nonaccident subjects. Twenty representative high-accident and nonaccident rate airmen were studied intensively, using individual clinical psychological and psychiatric techniques, as well as a number of measures of interest, intelligence, psychophysical skills, and psychophysiological functioning.

TABLE 4.—*Summary of Significant Differences Between Accident-Repeater and Nonaccident Groups on MMPI* and Social History Items*

Item	High	1955	1956	1957
MMPI*				
Go to church almost every week	N†	0.05	0.20	ns‡
Never did anything dangerous just for the thrill of it	N	0.20	0.20	ns
Frequently notice hand shaking when trying to do something	N	0.20	0.20	0.20
Used alcohol excessively	A	0.10	0.20	ns
Never been in trouble with the law	N	0.20	0.05	ns
When with a woman a man usually thinks about things related to her sex	A	0.01	0.20	ns
Pray several times a week	N	0.20	0.01	ns
Social history				
Single versus married	N	ns	0.10	0.20
No. of brothers	N	0.01	0.10	0.05
Drink to relax	A	...	0.20	0.10
Father attends church	N	0.10	0.01	ns
Desires to run away from home	A	0.01	0.20	0.10
Have ever been arrested (independent of traffic violations)	A	0.01	ns	ns

* MMPI = Minnesota Multiphasic Personality Inventory.
† N = Nonaccident; A = Accident repeater.
‡ Not significant below 0.20 level.

It is felt that the positive findings of the present study, particularly in the clinical area, contribute materially to a clearer understanding of the relation of psychological factors to accident susceptibility, at least in the population of airmen from which these samples were drawn.

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ALCOHOL IN THE SINGLE VEHICLE FATAL ACCIDENT

EXPERIENCE OF WESTCHESTER COUNTY, NEW YORK

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Records of motor vehicle accidents occurring over an eight-year period were used for the identification of all drivers killed in accidents involving neither other vehicles nor pedestrians. The resulting group of 117 drivers included 87 who died within four hours of their accidents. Postmortem determinations for alcohol were performed in 83 (95%) of these 87 cases. Of these 83, forty-one (49%) were found to have had blood alcohol levels of 0.15% or more at death; and an additional 17 (20%) were found to have levels between 0.05 and 0.15%. There is justification for assuming that any driver with a blood alcohol level of 0.15% or more is incapable of driving safely and that this is also true of many drivers with levels in the 0.05 to 0.15% range. It is therefore concluded that the use of alcohol was probably a causal factor in one half or more of the deaths which resulted from accidents of this type.

Estimates of the frequency of markedly elevated blood alcohol levels among those involved in motor vehicle accidents have ranged from 10 to 80%.[1] It is the purpose of this paper to report the findings of an exploratory investigation designed to quantitate more precisely this factor in a specific group of fatalities occurring in one area and to suggest that similar groups may prove useful for statistical purposes.

Most reports of the frequencies of such postmortem alcohol levels, a number of which have recently been summarized by Plymat,[2] have come from police and related sources. In general, with relatively few exceptions, these have failed both to reach the available scientific literature and to be presented in a sufficiently documented form to permit their complete evaluation from the scientific standpoint. Their value, as a result, is difficult to assess. Taken as a group, however, one or more of a number of substantial shortcomings appear to have been present in many instances. Foremost among these has been the frequent study of only relatively small fractions of the groups of fatalities whose characteristics these fractions were assumed to represent. Furthermore, it has been a not uncommon practice to group the persons killed without reference to their individual responsibilities for the collisions in which they were involved. In addition, some investigators have studied subjects who have died as long as 24 hours after the time of the accident, a procedure which has undoubtedly resulted in the inclusion of some whose original blood alcohol levels had undergone substantial metabolic lowering in the relatively long interval prior to death. Finally, information has often been omitted both as to the biological materials on which the determinations were based and as to the circumstances of their collection.

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In order to avoid these and related deficiencies, the retrospective and exploratory investigation reported here sought, as its primary objective, to determine the levels of alcohol present in the blood of a carefully studied group of drivers, those whose fatal accidents had involved neither pedestrians nor vehicles other than their own and who had survived for not more than a given short period after the event.

Case Material

The group which provided the subdivision used consisted of all motor vehicle fatalities which had occurred in Westchester County from Jan. 1, 1950, through Dec. 31, 1957. To assure completeness, the files of the Office of Vital Statistics in the New York State Department of Health were used to identify all deaths due to motor vehicle accidents in Westchester County during that period. The resultant lists were matched with those of the Office of the Medical Examiner. Of the 626 cases identified in this fashion, 37 were excluded. These consisted of 20 driveway and other off-highway motor vehicle fatalities and 17 borderline cases which, though they had occurred upon public roads more or less in association with motor vehicles, were not considered appropriate for inclusion. Illustrative of the latter group were such cases as those of a single pedestrian suicide and of two persons who fell after alighting from unmoving vehicles. The remaining 589 fatalities formed the basis of the present study.

Table 1.—*Classification of Motor Vehicle Fatalities by Age of Person and Type of Specimen Used for Alcohol Level Determination, Westchester County, New York, 1950-1957*

		Age 16 Years and Over					
			With Alcohol Level Determination		Specimen Used		
Class of Fatality	Total All Ages	Total	No.	%	Blood	Brain	Liver
Drivers	208	208	160	77	124	7	29
Single motor vehicle	117	117	95	81	76	4	15
More than one motor vehicle	84	84	58	69	44	3	11
Other and not specified	7	7	7	*	4	...	3
Passengers	197	184	107	58	97	1	9
Pedestrians	177	136	78	57	60	4	14
Others	7	1	0	*	...	...	...
Total	589	529	345	65	281	12	52

* Percentages based on less than 10 observations are not indicated.

Westchester, a wealthy county of 435 square miles located immediately north of New York City, includes urban, suburban, and semirural areas. According to the 1957 special census its population was 752,406, an increase of 126,590 over 1950. Although data are not available as to the number of residents holding driver's licenses, registrations of vehicles of all types are known to have increased during the same period from 213,000 to 308,000. No appreciable information was available either as to the number of miles driven within the county or as to the ways in which vehicles were used, although it is known that much of the traffic load is produced by nonresidents.

Alcohol Determinations

Of the 589 fatally injured persons, 345 (65%) had had alcohol determinations (table 1). Two hundred eighty-one of these were based on blood, 12 on brain, and 52 on liver specimens. These determinations were made with a modification of the Jetter method,[3] a procedure which measures volatile reducing substances, here taken as ethanol. Blood specimens consisted of heart blood drawn at autopsy, in almost all cases prior to the severance of the great vessels. No femoral or other peripheral blood specimens were used. In the several instances in which brain and liver alcohol levels were determined, parenchymal tissue was used. The values given for all specimens are the results of the laboratory determinations, although it is known that brain and liver alcohol levels tend to be substantially lower than the simultaneous blood concentrations.[4] For this reason, the group of liver and brain alcohol values given here may be regarded as a conservative estimate of the blood alcohol levels to which they corresponded.

As noted, postmortem alcohol determinations had been carried out in only a fraction of cases, and only rarely among those under 16 years of age. However, even when limited to those 16 years of age and over, determinations were found to have been performed in the latter group least often for pedestrians (57%) and passengers (58%) and most often for drivers (77%). As a result of the relatively large percentages of these groups lacking determinations, it was not felt that estimates of the distributions of alcohol levels among their numbers could be made without further subdivision.

Results

The total group of 589 motor vehicle fatalities was first analyzed in order to determine whether or not there had been any significant changes over the eight years represented. The variations in the total number of fatalities from year to year proved not to be statistically significant ($p>0.10$). In addition, the variations from year to year by type of accident, class of vehicle involved, class of fatality, and age or sex of the deceased all proved to be not statistically significant ($p>0.10$).

The data for the eight-year period were therefore combined and treated as a single group. When handled in this fashion, there was no statistical significance in the variation in the number of fatalities from month to month ($p>0.70$). However, as anticipated from many prior reports, many more fatalities occurred during the two and one-half day period between 5 p. m. Friday and 5 a. m. Monday than during the remainder of the week. This is seen in the fact that 277 (48%) of the 573 fatalities for which complete information was available with regard to time and day of accident fell in this 60-hour week-end period. In addition, when distributed by time of day, it was found that 63% of the 573 fatalities resulted from accidents which occurred between 5 p. m. and 5 a. m.

Table 2.—*Blood Alcohol Level and Interval Between Accident and Death for Fatally Injured Persons Sixteen Years of Age and Over, with Blood Alcohol Level Determinations, Westchester County, New York, 1950-1957*

Alcohol Level, % by Weight	Total	Interval Between Accident and Death, Hr. <4	4-11	>11	Not Specified
Negative	147	117	21	9	...
0.01-0.04	13	10	2	1	...
0.05-0.09	23	19	3	...	1
0.10-0.14	15	15	...	...	...
>0.14	83	79	3	. .	1
Total	281	240	29	10	2

As has been noted, alcohol levels were not determined for all fatally injured persons. Since the minimum licensing age in New York is 16, and since alcohol determinations were rarely carried out on children, the data given in tables 2 and 3 were restricted to include only fatally injured persons 16 years of age and over. From table 1, it is noted that this restriction did not reduce the number of drivers used in this study, since not one of the 208 drivers in the total group of 589 fatalities was under 16.

In order to avoid the reporting of postmortem alcohol levels which had been subject to substantial metabolic lowering during the period between accident and death, it was decided to consider only those persons who had died within four hours of their accidents. Table 2 indicates the effect of this restriction on the composition of the group retained for study purposes.

It was initially believed that the study of those drivers who had had alcohol determinations would make possible the ascertainment of whether or not the levels found in heart blood might have been influenced by diffusion of alcohol from the viscera. Since it was reasonably expected that the presence and magnitude of this possible artifact would be a function of the interval between death and the drawing of the specimen at autopsy, the levels were grouped according to the time which had elapsed before the collection of each individual specimen. In doing this it was observed that most of the cases with the longer intervals between death and postmortem examination were those of individuals who, in being killed as the result of evening and early morning accidents, had not had autopsy performed until the next working day. As a result, the group whose examinations had been most delayed was heavily weighted with cases from that period of day in which a higher percentage of drivers had been drinking and in which relatively higher alcohol levels were present. Because of this selection, it was not possible to demonstrate the presence or absence of an artifact of this type, the possible significance of which is discussed below.

During the eight years studied, 87 single vehicle accidents occurred which involved neither pedestrians nor other vehicles and as the result of which the driver in each case died within four hours of the accident. It will be recalled that it was the description of the blood alcohol levels of this group which constituted the primary objective of this investigation. Fortunately, because of a long-standing interest of the Office of the Medical Examiner [5] in the extent to which alcohol was present among driver fatalities, 83 (95%) of this group had had alcohol level determinations. The resultant data are presented in table 3.

The results given in table 3 show that 41 of the 83 "single vehicle" drivers examined possessed blood alcohol levels of 0.15% or more at the time of death. These constituted 49% of the group. The levels of an additional 17 of this group (20%) fell between 0.05 and 0.15%. In comparison only 22 (27%) were negative. It is noted that the 83 drivers included 7 truck operators, all men, and 6 women operators of passenger automobiles. Of these, one of the former and three of the latter had levels of 0.15% or higher.

Previous Research

The improper use of alcohol as a cause of motor vehicle accidents has been repeatedly reported from many regions of the earth, including Canada, Scandinavia, Germany, France, Italy, the United Kingdom, South Africa, Australia, and the United States. (The *Quarterly Journal of Studies on Alcohol* contains abstracts of technical papers concerned with alcohol, including, in particular, many dealing with motor vehicle accidents.) In view of this, it is remarkable neither that much basic research has been completed nor that much remains to be done.

Table 3.—*Alcohol Level by Type of Specimen in Eighty-seven Drivers Involved in Single Vehicle Accidents Who Died Within Four Hours of Accident, Westchester County, New York, 1950-1957*

Specimen Used	Total	Alcohol Level, % by Weight Negative	0.01-0.04	0.05-0.09	0.10-0.14	>0.14	No Examination
None	4	...	...	...	...	...	4
No. examined	83	22	3	11	6	41	...
Blood	66	16	2	6	2	40	...
Brain*	3	1	...	...	2	...	...
Liver*	14	5	1	5	2	1	...
Total	87	22	3	11	6	41	4

* Values shown are actual results of laboratory determinations. Values for brain and liver specimens have not been adjusted for known differences between tissue and blood levels (see text).

In general, research dealing with this problem has largely fallen into two categories: (1) the determination of the extent to which accident liabilities increase in association with blood alcohol level and (2) the determination of the extent to which individuals with such elevated levels are responsible for accidents. Although the present paper is concerned with the second of these research areas, it is appropriate to indicate briefly the findings of the first and to suggest sources of additional information.

Thus, for example, Loomis and West[6] in a recent study with use of "a simulated automobile driving apparatus . . . to evaluate the effect of alcohol as it pertains to several functions involved in driving an automobile," have demonstrated "a direct relationship between the blood alcohol concentration and the extent of impairment of function." Furthermore, these workers found that (1) all of the eight subjects (apparently none of them heavy drinkers) who were tested when their blood alcohol levels were "at or above 0.05% showed some impairment as compared to their control performance," (2) the two subjects who were tested when their blood alcohol concentrations were 0.03% showed performance below control values, and (3) "in the presence of a blood alcohol concentration of 0.15 per cent performance had decreased to approximately two-thirds of the control values."[7]

Other workers, notably Coldwell and others, in "Report on Impaired Driving Tests,"[1] and Bjerner and Goldberg,[8] used objectively scored driving tests given to subjects before and after the use of beverage alcohol. In the most recent of these,[1] 50 adult male subjects, including 5 who "habitually consumed, each day, alcoholic beverages equivalent to at least 6 fl. oz. of distilled spirits" and 5 who "consumed twice this quantity daily," repeatedly drove through a standardized test. The many results of this investigation included (1) the finding of one individual whose performance was impaired at a venous blood alcohol level of 0.04%, (2) the demonstration that one-half of the 50 subjects showed objective impairment of driving ability at a venous blood alcohol concentration of 0.08%, and (3) the finding that all subjects exhibited some evidence of impairment at levels less than 0.15%. The authors pointed out that the men were in a competitive situation which placed a premium on optimum performance and that the test was relatively simple, presenting neither the emergencies nor other hazards present in normal driving.

Two additional studies require mention. In the first of these,[9] by the comparison of the blood alcohol levels of 433 drivers involved in accidents with those of 2,015 driver passers-by, three conclusions were reached: "1. The hazard is significant when the blood alcohol concentration is above 0.10%. 2. In the range 0.10-0.15% blood alcohol concentration, the hazard of accident is two and one-half times that when the concentration of alcohol in the blood is less than 0.05%. 3. This hazard of accident when blood concentrations are above 0.15% is approximately 10" (i. e., there were 10 times as many drivers with levels of 0.15% and above in the accident-involved group as in the control group of uninvolved drivers). The second study,[10] through the use of samples obtained from 542 of 919 drivers involved in personal injury accidents, compared the blood levels of those rated highly responsible for the accidents in which they were involved with the levels of those rated as either not responsible or only slightly so and demonstrated an increasing statistical excess of accident-responsible drivers which first became significant in the 0.03 to 0.05% range. Additional research[11] conducted in Sweden, with appropriate controls, has shown that chronic alcoholics and other alcohol abusers were heavily overrepresented in a consecutive series of 2,100 persons convicted of drunken driving.

We do not intend to imply by the title and content of the present paper that we regard the presence of alcohol as the only pertinent characteristic of the individuals described. It might be expected, in fact, that other personal characteristics, themselves associated with individual drinking patterns, would also be related to accident liability. The results of another well-controlled Swedish investigation are of some interest in this connection, however. This study[12] of 71 hospitalized traffic victims showed that, although heavy users of alcohol were highly overrepresented among casualties who had been drinking, they were not overrepresented among those casualties who had not been drinking. These results suggest that the changed liability which the heavy user group exhibited was very closely associated with, if not directly caused by, the use of alcohol.

Medicolegal Interpretations of Blood Alcohol Levels

In the United States, the Uniform Vehicle Code, Model Chemical Test Law, used (July 1, 1957) in 27 of the 48 states,[13] defines (Article IX, Section 11-902) the following presumptions: 1. If there was at that time 0.05% or less by weight of alcohol in the defendant's blood, it shall be presumed that the defendant was not under the influence of intoxicating liquor. 2. If there was at that time in excess of 0.05% but less than 0.15% by weight of alcohol in the defendant's blood, such fact shall not give rise to any presumption that the defendant was or was not under the influence of intoxicating liquor, but such fact may be considered with other competent evidence in determining the guilt or innocence of the defendant. 3. If there was at that time 0.15% or more, by weight, of alcohol in the defendant's blood, it shall be presumed that the defendant was under the influence of intoxicating liquor. (Although there is much individual variation, and although many factors influence the rate of absorption of alcohol and the levels achieved, it is commonly stated that "In order to obtain a blood alcohol level of 0.05% a 150-lb. (68-kg.) person would have to accumulate 1 fluid oz. (30 cc.) of pure alcohol in his body. To do this he would have to drink at least the equivalent of 2 oz. of 100 proof liquor. This same person would have to accumulate 3 oz. of absolute alcohol to reach a blood alcohol level of 0.15%." [14]) 4. The foregoing provisions shall not be construed as limiting the introduction of any other competent evidence bearing upon the question whether or not the defendant was under the influence of intoxicating liquor.

This corresponds to the position of the American Medical Association, which has long endorsed the same limits, "limits (which) were purposely made liberal so that no injustice would be done to the person with unusual tolerance." [15] Nevertheless, proposals for a lowering of the 0.15% limit to 0.05% have been made.[16] It is pertinent, in this respect, that at a 1952 "meeting of Scandinavian criminologists held in Copenhagen . . . the representative of Norway (which has long enforced the 0.05 per cent limit) . . . criticized the Norwegian . . . limit very strongly" on the grounds that it placed undue emphasis on "a chemical determination." The latter position was not supported, however, by "other Norwegian members of the conference." [17]

Significance of Data

With the foregoing findings as background, it was not considered necessary to prove again that the use of alcohol is a causal factor in some motor vehicle accidents. Furthermore, it was not considered necessary to demonstrate once more that there are substantial differences between the distributions of the alcohol levels among accident-involved drivers and those of the driving populations from which they come. It was the purpose, therefore, of the investigation reported here to determine the extent to which individuals with levels already demonstrated to be associated with markedly increased liabilities were present in a group of drivers killed in single vehicle accidents without pedestrian involvement. Fatally injured persons of this type constitute the only group of persons on whom autopsy is performed who may be regarded without additional evidence as having been responsible in most cases for the accidents which cause their deaths. This group offers, as a result, opportunities for study which are not present when pedestrian and multivehicle accidents are considered, since information concerning the principals (i. e., all involved drivers and pedestrians) in, and circumstances of, such events is seldom complete. It also requires neither the personnel nor the expenditures which are required for the collection and analysis of specimens from the principles involved in the more complex varieties of accidents.

An additional reason for choosing one accident type stems from the increasing tendency in this field to compare the alcohol levels found among accident-involved drivers and pedestrians in different communities and jurisdictions. Unfortunately, such comparisons have frequently grouped together dissimilar types of accidents and, in addition, have compared groups of data weighted with those particular combinations of accidents most common in each area considered. If such inevitable comparisons are to be made, it would appear essential that, whenever possible, they be based on the use of careful breakdowns into similar accident categories, since it would be expected that the causes of accidents might vary considerably from one type to another. It is suggested, therefore, that the alcohol levels found in drivers in the "single vehicle group," as used and defined in this paper, may serve as the basis of one form of comparison between jurisdictions which have sufficient fatalities to allow their subdivision to this extent.

This proposal for the use of comparisons based on the levels found in this group is based, as has been noted, on a number of practical limitations in the extent to which inferences may be founded on examinations of motor vehicle fatalities. As such, it too has limitations. The first of these results from the fact that knowledge in this field is so incomplete that it is at present seldom possible to extrapolate quantitatively from fatal to nonfatal accidents or the reverse, a point which is commonly overlooked. In addition, quantitative extrapolations from the single vehicle group to pedestrian and multivehicle accidents must also await the results of additional research dealing with these groups, although it is well known that many of the multivehicle and pedestrian accidents which have occurred in Westchester and elsewhere have been caused by drivers and pedestrians who were drunk at the time.

It should be noted in this context, however, that related information has long been available concerning the experience of one community, Uniontown, Pa., with another group of drivers presumably responsible for the accidents in which they were involved. Thus, Heise found, in a pioneering investigation reported in 1934, that the alcohol levels of a consecutive series of six apprehended "hit and run" drivers fell between 0.21 and 0.38%, the mean value being 0.30%. By contrast, on the basis of 119 consecutive accidents, he also concluded with respect to pedestrian accidents that "the drivers who struck children or old people were in most cases sober," and that "the largest number of accidents in this group . . . [involved] the drinking pedestrian." [18] This again suggests the need for the careful separation of accidents into discrete categories and the caution which should be used in attempting extrapolations from one group to another.

The limitation of the present series to those dying within four hours of their accidents was based on a compromise between the relatively rapid rate at which alcohol is known to be metabolized [10] and the need for including as many cases as possible in order to facilitate their analysis. In recognizing that the levels in many individual cases have been shown to remain elevated for much longer periods after ingestion than this,[19] it must nonetheless be remembered that many of those killed may well have already been on the descending slopes of their blood alcohol curves at the times of their accidents. For this reason, the four-hour interval is believed to represent a conservative compromise, one that is also supported by the fact that the levels found among those who had died between 4 and 12 hours after their accidents tended to be lower than those found among persons who had died in a shorter time. It is of further interest that 219 of those listed in table 2 had died within two hours and 199 within one hour of their accidents, a point which also has significance from the standpoint of the organization and emphasis of emergency medical care.

It has been mentioned that heart blood had served as the basis for most of the alcohol determinations on which this study was based and that no femoral or other peripheral specimens had been used. This point is emphasized because of the considerable literature dealing with the meaning and relationships of alcohol levels as determined from various portions of the cardiovascular system.[20] Thus, it has long been known that during the stage of active absorption of alcohol from the gastrointestinal tract the levels present in the venous return from the limbs may be considerably lower than those found in blood drawn from the heart, a difference which is attributed to the comparatively long time required for the levels in the relatively avascular tissues of the extremities to come into equilibrium with those of the arterial blood.[4] In addition, Gifford and Turkel have demonstrated in a series of 11 cases that whiskey introduced into the stomachs of nonalcoholic cadavers on which autopsy was performed 10½ to 24 hours later consistently produced alcohol levels in heart blood. This suggested that similar false elevations might occur in the heart blood of fatally injured persons whose viscera contained high concentrations of alcohol as the result of the use of alcoholic beverages shortly before death. Since these workers also demonstrated in this series that diffusion into the femoral blood was negligible, it became possible for them to compare individual postmortem heart and femoral alcohol levels in an investigation of the extent to which such an artifact might be present in actual practice. This was done in a series of 51 alcoholic cadavers. The results indicated that the discrepancy sought might prove of considerable medicolegal importance in occasional cases. It was also demonstrated, however, that the average excess of the heart blood alcohol level over that found in the femoral vein was slightly less than 0.01%.[20b] In view of the latter finding, it is considered improbable that such a diffusion artifact had to any appreciable extent influenced the alcohol levels given in the present report.

The results of the investigation reported here show that at the time of death 49% of the drivers killed in single vehicle, nonpedestrian accidents possessed blood alcohol levels of 0.15% or more by weight. These levels are widely accepted on the basis of a considerable body of scientific knowledge as presumptive evidence of drunken driving. An additional 20% of the drivers in this group possessed levels between 0.05 and 0.15%. As discussed above, it has been shown that many persons with levels in this range not only exhibit measurable deteriorations in driving performance but also are overrepresented in accident groups.

In view of these findings from Westchester County, it is appropriate to question the extent to which similarly elevated levels might be found elsewhere in fatally injured persons of this type. Fortunately, one set of data already existed which was indicative of the somewhat comparable experience of another section of the United States. Thus, the Delaware State Police have studied all fatal accidents occurring each year at locations outside of the city of Wilmington, with particular reference to the alcohol levels of most principals. As a result it has been possible, on the basis of data made available to us through the courtesy of the Delaware authorities,[21] to identify a group of fatally injured drivers similar to the single vehicle drivers studied in this report. This group consists of the 15 fatally injured drivers during 1957 whose passenger automobile accidents involved neither pedestrians nor other vehicles and who were listed as having died either at the scene of the accident or prior to arrival at the hospitals to which they were taken. Ten (67%) of this group were found to have blood alcohol levels of 0.15% or more, and two had levels between 0.10 and 0.15%. These data suggest that the high alcohol levels observed among drivers killed in single vehicle accidents in Westchester County may exist in other sections of the United States.

In conclusion, it is recalled that Heise stated in 1934 "that the problem of controlling the drinking driver and pedestrian is far from being solved may be due, in part, to the fact that no accurate statistics are available regarding the relationship of alcohol to automobile accidents. . . ."[18] On the basis of the findings presented in this report and previous work in this field, it appears highly probable that the use of alcohol was a causal factor in the deaths of one-half or more of the drivers killed in the single vehicle accidents which occurred in Westchester County over an eight-year period.

Summary

The postmortem blood alcohol levels were studied in a group of 83 drivers whose fatal accidents involved neither pedestrians nor other vehicles and whose deaths followed within four hours.

Forty-nine per cent of the 83 were found to have had blood alcohol levels of 0.15% or more at death, while those of an additional 20% fell between 0.05 and 0.15%. From this and previous studies it is concluded that it appears highly probable that the use of alcohol was a causal factor in the deaths of one-half or more of the drivers killed in the single vehicle accidents which occurred in a suburban county over an eight-year period.

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The authors wish to express their appreciation to Mr. Andrew Frey and Mr. Morton Berk for performing the many chemical analyses on which this report is based. They also wish to thank Mrs. Helen C. Chase and the staffs of the Driver Research Center and the Office of the Medical Examiner for their most generous assistance.

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CARBON DIOXIDE POISONING.—Although rarely reported, carbon dioxide poisoning is probably not so infrequent an occurrence. . . . Early in March, 1956, a liner arrived at Penang with a cargo of onions. The particular hold had been loaded six days previously, and contained 5,000 bags of onions and a quantity of . . . a crude brown sugar obtained from the sap of palm trees. It was full to within 9 ft. (2.7 m.) of the deck. At about 1 p. m. the ship was boarded by labourers, who removed the hatch covers and opened the hatch. One entered the hold and collapsed as he was standing on the onions. Another went in to help him and also collapsed. Then the ship's doctor was sent for; he went into the hold, followed by one of the ship's officers, and assisted him to lift the unconscious man who had first entered the hold. As he was doing so the doctor collapsed, and the ship's officer carried the man out. One of the ship's crew then went into the hold to assist, but he collapsed. Another ship's officer then entered with breathing apparatus, and brought out the doctor and the other unconscious men. The four men who had collapsed were then taken to hospital, where it was found that two of them were dead. Four other labourers who had also entered the hold for short periods developed minor symptoms and were taken to hospital. . . . An analysis of the gases present in the hold was carried out by the senior chemist about an hour and a half after the hold had been opened. He obtained an appreciable reaction for carbon dioxide in the hold, particularly beneath the deck; and on examining other holds in the ship, as yet unopened, he obtained a strong reaction. No other poisonous gases were detected.—H. I. Williams, M.D., B.Chir., Carbon Dioxide Poisoning, *British Medical Journal,* Oct. 25, 1958.

POSTERIOR COLPOTOMY INCISIONS IN GYNECOLOGIC DISEASE

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Posterior colpotomy has the advantage over culdoscopy and colpocentesis in that it gives much more diagnostic information. It is safer than anterior colpotomy, which has to be done with special care to avoid the bladder, ureters, and perivesical venous plexuses. Moreover, by extension of the incision after diagnosis and using proper retraction, considerable pelvic surgery can be accomplished. Colpotomy was carried out in 94 women, the most frequent indication being ovarian cyst (29 cases). In the technique which is described, a posterior incision was used in all but two cases. The most frequent findings were ovarian cyst (34 cases) and pelvic inflammatory disease (17). Recovery was uncomplicated in 84 cases; five patients had postoperative complications and five others subsequently underwent laparotomy. The results justified the procedure, which is less traumatic than exploratory laparotomy and can be used in many situations in which an exploratory laparotomy is not really indicated.

With the increased interest in vaginal hysterectomy and vaginal surgery in general in the past 25 years, the use of a posterior, and occasionally an anterior, incision of the vaginal wall for exploration of the pelvis should be more widely known and practiced. Posterior colpotomy has been disregarded for many years as either a diagnostic or a therapeutic measure in gynecology. The literature of 50 or 60 years ago contains numerous papers on this subject. The primary reason for the disuse of the procedure has been the increasing safety of an anterior abdominal wall incision. Such an incision provides maximum exposure in the pelvis, and it is this improvement in exposure and the allowance for wider surgical performance that has led to the abandonment of colpotomy as a popular procedure. Posterior cul-de-sac puncture (colpocentesis) and culdoscopy have, however, enjoyed some measure of interest in recent years, and in view of modern medical economics, improved techniques in anesthesia, and the generalized use of antibiotics it is important to reconsider the use of colpotomy incisions in gynecologic diagnosis and therapy.

The term colpotomy covers three procedures. In the first, puncture colpotomy, a needle or trocar is used in the posterior cul-de-sac for intraperitoneal aspiration. This is in reality a colpocentesis. The second is a small posterior cul-de-sac incision for the intraperitoneal insertion of the culdoscope. The third is a wide incision (3 to 6 cm.) penetration of the posterior cul-de-sac into the peritoneal cavity. This can be accomplished anteriorly under the bladder but with greater difficulty.

The advent of the culdoscope has made possible the use of the posterior cul-de-sac as an avenue of exploration for diagnosis in the pelvis. This is primarily a diagnostic instrument, although Decker has reported using it for ovarian biopsy and the collection of an ovum at the time of ovulation.[1] While culdoscopy is a great improvement over colpocentesis, it entails the added difficulty of proper positioning of the patient for adequate examination. This is no easy task in many instances. Also, the reversal of the normal position of the pelvic organs, as seen through the culdoscope, occasionally gives a distorted pathological impression, and the magnification of the lenses of the instrument often gives a false interpretation of the pelvic findings. It is, however, a fine diagnostic tool, and its use is more feasible for diagnostic procedures in the pelvis generally than colpocentesis. Culdoscopy has been carried out in office practice, but this is not recommended.

Diagnostic information obtained by colpocentesis is much more limited. By this method different kinds of fluid from the abdominal cavity can be obtained through a needle or trocar. This is a very confined diagnostic medium and, in fact, is often unreliable. The dangers inherent in blind puncture of the cul-de-sac and the undependability of findings have led to the condemnation of the method by many gynecologists. The primary therapeutic use of colpocentesis is drainage of a cul-de-sac abscess. The number of procedures that can be accomplished through either a posterior or anterior colpotomy approach is far greater than that possible with either colpocentesis or culdoscopy.

Methods

There are two types of difficulty that may arise in connection with colpotomy: preexisting factors rendering exposure difficult, and surgical complications. Among the anatomic causes of preexisting difficulty are obesity; contracted vagina (long, narrow, small, and senile); virginal inlet; nulliparous inlet; and pregnancy. Pathological causes of pre-

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existing difficulty include pelvic adhesions (pelvic inflammatory disease or endometriosis); pelvic carcinoma; uterine and cervical myomas; intestinal tumors; and solid ovarian tumors. Possible intraoperative surgical complications include perforation of the intestine (usually of the rectum); spillage of intestinal contents; ovarian cysts (dermoid or malignant); hemorrhage; and, with anterior colpotomy, injury to the urinary tract. Possible postoperative complications include intraperitoneal and extraperitoneal hemorrhage; vaginal cuff hematoma; infection; and painful vaginal scar.

In general, contraindications to colpotomy include severe chronic pelvic inflammatory disease; extensive intra-abdominal adhesions; endometriosis; ruptured ectopic pregnancy (with patient in shock); large intra-abdominal tumors; known ovarian carcinoma; and cases in which the cul-de-sac is not obviously free.

Ninety-four patients were subjected to colpotomy. A listing of the procedures accomplished follows. These patients came from private practice, the U. S. Army Medical Service, and the University of Oregon Medical School Hospitals and Clinics. The method was adopted in order to evaluate its applicability to modern approaches in gynecologic diagnosis and treatment. Certain observations were proposed in order to do this. The technique used was a simple one, similar to that of Bradbury.[2]

Technique.—With the patient in position as for lithotomy, the posterior cul-de-sac is identified and traction put on the vaginal mucosa with an Allis tissue forceps placed near the cervix, which is also on traction (fig. 1). A transverse incision from 3 to 6 cm. in length is made in the vaginal mucous membrane (fig. 2), the peritoneum is identified and entered (fig. 3 and 4), and the lip of the posterior retractor is placed in the peritoneal opening, which may be retracted anteriorly with use of a Deaver retractor. The uterus is then retroflexed for better exposure when necessary. On conclusion of the pelvic exploration or surgery, the peritoneum is closed (fig. 5) with a purse-string suture of fine chromic catgut. The vagina is then closed (fig. 6) with a running suture of the same catgut. Usually no packing is placed postoperatively, but this may be done if there is excessive oozing.

In this series the posterior incision was used throughout, with the exception of an anterior approach to an anterior ovarian cyst in one case and to an unruptured ectopic pregnancy in another.

Procedures Performed.—In the 94 women in this study on whom colpotomy was performed, there were many different indications for this operation. They included known ovarian cyst (29); known ectopic pregnancy (3); adnexal mass (18); tubal ligation (10); and miscellaneous (6). On the basis of general diagnosis alone 14 patients underwent the operation, and in 18 it was performed as part of an infertility study.

Posterior or anterior colpotomy with a large incision allows for maximum maneuverability and a wide choice of diagnostic and surgical therapeutic procedures. It enables the operator to make a satisfactory and complete diagnosis in the pelvic area. There is no distortion by magnification, and the organs are in their normal relationships. Diagnostic procedure or surgical intervention does not necessitate any change of position or draping. The incision can always be extended, if necessary, and with proper retraction considerable pelvic surgery can be accomplished.

The following are procedures carried out in this series: (1) exploration of the pelvis for differential diagnosis; (2) salpingectomy, unilateral and bilateral; (3) resection of ovarian cyst, unilateral and bilateral; (4) oophorectomy, unilateral and bilateral; (5) bilateral wedge resection of the ovary; (6) lysis of ovarian, tubal, uterine, intestinal, peritoneal, and omental adhesions; (7) visualization of the appendix and cecum; (8) evacuation and drainage of large ovarian cystic structures; (9) infertility studies (including direct observation of the ovary, for example, to see and perhaps even perform a biopsy on a corpus luteum; observation of fallopian tubes with injection of methylene blue to determine patency; removal of previously placed plastic tubes and hoods; tubal plastic operations; and observation of ovulation); (10) sacrouterine neurectomy; (11) sacrouterine plication for third-degree retroflexion and retroversion; (12) Pomeroy's operation (ligation and resection of fallopian tubes); (13) removal of ectopic pregnancy, ruptured and unruptured; (14) excision of enlarged cysts of Morgagni; and (15) removal of pedunculated myomas.

Anterior colpotomy can also be done for anterior ovarian cyst or for ectopic pregnancy which cannot be brought down into the posterior incisional area. This involves more dissection but can be done without great difficulty when the patient is a multipara. Particular attention to anatomy, especially to the bladder and ureters, and care in making the incision sufficiently wide, are factors which facilitate the anterior approach. It is advantageous to be able to use the anterior approach under certain circumstances; for example, in a situation in which it is not possible to turn the uterus into retroversion, when this is needed. Care must be taken to avoid the bladder or ureters as well as the perivesical venous plexuses.

Findings and Results.—At colpotomy were found ovarian cysts (34); ectopic pregnancies, ruptured (3) and unruptured (2); pelvic inflammatory disease (17); postoperative adhesions (6); endometriosis (5); and myoma (1). In 30 patients no gynecologic disease was found. Of the 14 patients who underwent colpotomy on the basis of general diagnosis alone, 2 had ectopic pregnancies; 2, ovarian cysts; 3, pelvic inflammatory disease; 2, postoperative adhesions; and 5, no gynecologic disease. Of the 18 patients in

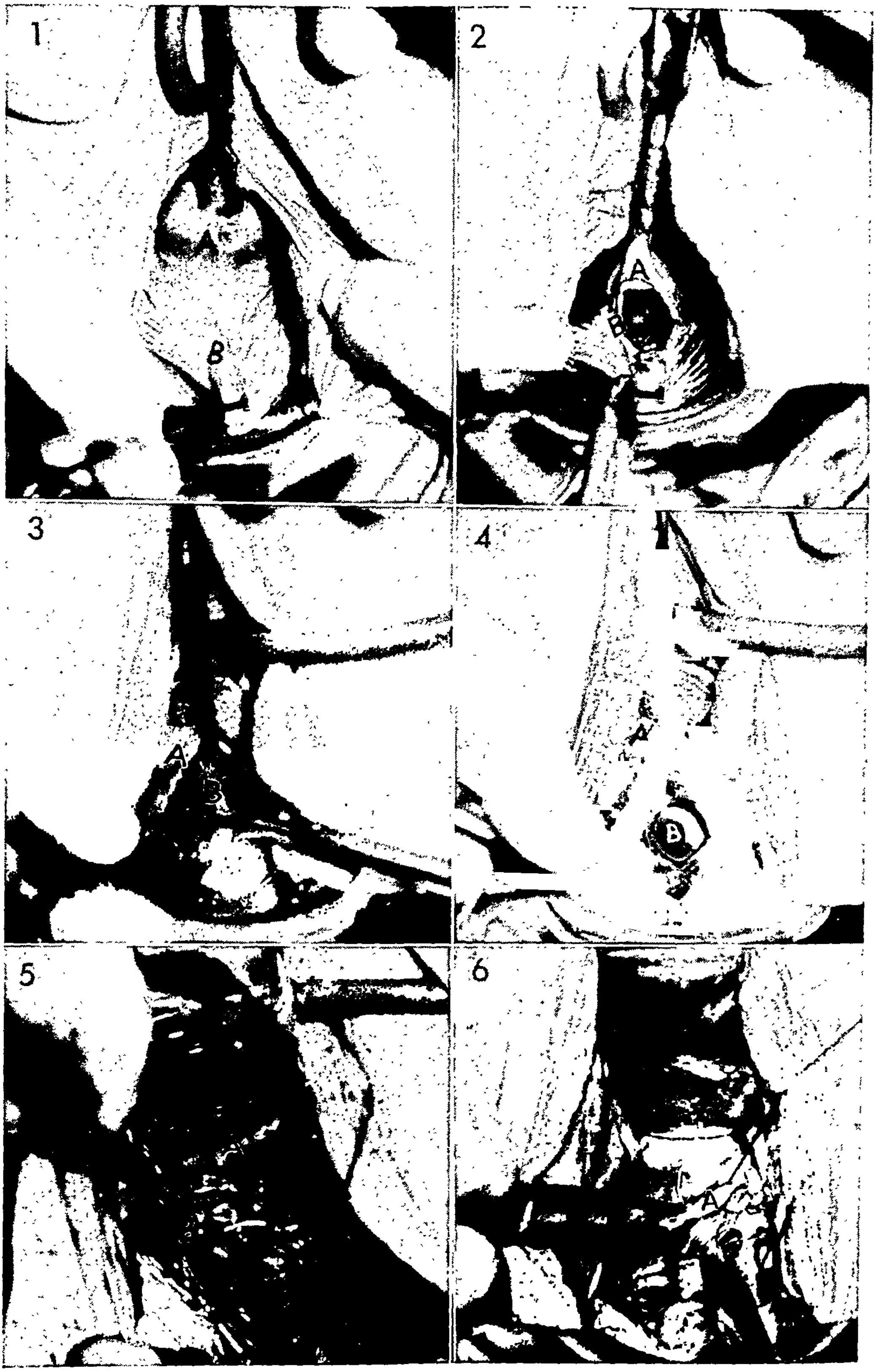

Fig. 1.—Exposure of posterior cul-de-sac. *A*, cervix; *B*, posterior vaginal mucosa. Fig. 2.—Incision in vaginal mucosa. *A*, vaginal mucous membrane; *B*, incision. Fig. 3.—Scissors incision of peritoneal membrane. *A*, vaginal mucous membrane; *B*, peritoneum. Fig. 4.—Incision through peritoneal cavity, later extended as necessary. *A*, vaginal mucous membrane; *B*, peritoneal cavity opened. Fig. 5.—Purse-string suture for closure of peritoneal incision. *A*, vaginal mucous membrane; *B*, peritoneal edge. Fig. 6.—Vaginal mucous membrane, closed with running suture. *A*, membrane.

whom the indication for colpotomy was the presence of an adnexal mass, 2 had ovarian cysts; 14, pelvic inflammatory disease; and 2, endometriosis.

The 34 ovarian cysts found in the sample were classified as follows: dermoid, 3; pseudomucinous cystadenoma, 1; fibroma, 1; endometrioma, 2; polycystic disease, 5 (inflammatory, 4; Stein-Leventhal, 1); Morgagnian, 1; corpus luteum, 10 (5 with and 5 without hemorrhage); and follicle, 11 (3 with and 8 without hemorrhage).

Of the 94 patients in the sample, 84 had an uncomplicated recovery. Five developed postoperative complications and five subsequently underwent laparotomy. The entire procedure was unsuccessful in only three. The average postoperative stay in hospital for all patients was three and one-fourth days. The results are a justification of the procedure, which is less traumatic than exploratory laparotomy and can be used in many situations in which an exploratory laparotomy is not really indicated.

Comment

The primary value of colpotomy is investigation of the pelvis by direct exploration without laparotomy. It is of further importance that such exploration can be followed by surgical therapeutic measures at once from below. It is especially useful in relation to tubal and ovarian disease. It has a specific use in the observation and treatment of symptomatic, persistent, small ovarian cysts in young women. These smaller masses have been a matter of concern to gynecologists for a long time, because when the final diagnosis and treatment of these masses indicates an abdominal incision, it is not a minor matter. Many ovarian cysts can be observed, resected, or removed through a posterior colpotomy incision, thus eliminating the necessity for abdominal exploration.

It is unfortunate that one of the least diagnosed diseases in gynecology is ovarian cancer. More frequent use of the posterior colpotomy incision facilitates the early diagnosis of this disease, because one of the most valuable aspects of the procedure is the direct observation of ovarian tissue. The presence of a solid or questionable tumor is an indication for laparotomy. If the cyst should prove to be innocent, it often can be removed vaginally. Intraperitoneal fluid can be aspirated and spun down to verify an unusual or questionable lesion whenever indicated. What is most important is that, since this is relatively a less complicated procedure than the abdominal exploratory operation, familiarization with its use will lead to earlier and more frequent intraperitoneal investigation of ovarian masses. Conservation of the ovary is the best practice except when such conservatism leads to the preservation of an ovarian cyst for an extended length of time, bringing about eventual necrosis of ovarian tissue.

Another important application is that it is possible, when a diagnosis of mild pelvic inflammatory disease is made, that lysis of tubal adhesions can be accomplished, thus occasionally making it possible to establish tubal continuity or to prevent the continued formation of adhesions which permanently destroy the tube.

In the presence of other pelvic disease, posterior colpotomy can easily be converted to vaginal hysterectomy or pelvic repair, if such procedure should be indicated at the time of surgery. It has long been a practice of a well-known gynecologist (Dr. Allen of Chicago) to do a posterior colpotomy, along with a dilation and curettage, prior to every vaginal hysterectomy. This simple transvaginal incision has been extended in this series to include sacrouterine neurectomy in cases of dyspareunia, dysmenorrhea, pelvic pain, and some cases of infertility.[3] Section of the sacrouterine ligaments can be done to enlarge the incision. Plication of these ligaments without section can be done for the prevention of enterocele.[4] The transvaginal approach to the peritoneal cavity has great value for women, correctly or incorrectly labeled hysterical or neurotic, who manifest a desire for repeated abdominal operations for vague pelvic or abdominal pain. In these instances it is of great help to be able to eliminate doubt as to real or fancied pelvic disease.

It has long been felt that the freeing of one set of adhesions through an abdominal incision has merely served to create another set. Yet there are many individuals who are relieved for a long time by the lysis of pelvic or postoperative abdominal adhesions through a colpotomy. The same is true in an apparently symptomatic pelvic condition in which a definite diagnosis of uterine or adnexal disease cannot be made. The symptoms are often of a nature which makes it impossible to examine or evaluate these patients adequately. In such patients the use of the posterior colpotomy is valuable not only in obtaining factual knowledge but also for psychological reasons. The use of the operation in these cases provides a simple and satisfactory exploration for diagnosis without involving the patient in an abdominal laparotomy. Its advantages over laparotomy are that it is, by contrast, a minor procedure; that postoperative convalescence is much shorter; that postoperative discomfort and complications are greatly reduced; that there is less tissue trauma; that symptomatic, intra-abdominal adhesions are fewer postoperatively; that the time required for the procedure is less; and that the operating room set-up is the same as for simple dilation and curettage.

The use of posterior or anterior colpotomy is by no means a panacea in gynecology, but it does have major advantages as a diagnostic and therapeutic tool which have been overlooked for too long. Its use can contribute in great measure to early diagnosis of ovarian carcinoma. It also permits many gynecologic diagnostic and surgical procedures to be accomplished at far lower cost and with much less hospitalization than are involved in exploratory laparotomy.

3181 S. W. Sam Jackson Park Rd. (1).

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FUNCTIONAL FASHIONS FOR THE PHYSICALLY HANDICAPPED

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The need of specially designed garments for physically handicapped people is becoming evident from the statistics regarding various types of disability in this country. The need can be met by a constructive program. Examples are given of clothing that is easy to put on, wear, and take off, that resists the friction of crutches and the strain of laundering, and that improves the morale of severely disabled persons. A coat-dress and a suit-dress for women and slacks for men are described in some detail. Continued research on patterns and fabrics is necessary. Problems of direct mail selling must be solved. Concerted effort in this field will help to overcome existing difficulties in the way of self-help, vocational rehabilitation, and social adjustment for millions of handicapped people.

As the result of a three-year research program, physically handicapped persons now have available for the first time a number of specially designed garments which combine fashion with function. The project had its inception when Mrs. Helen Cookman, a top "name" designer in fashion circles, was invited to become the consultant in clothing for the disabled to the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center.

Prior to this time, the occupational therapy division of the Institute of Physical Medicine and Rehabilitation had been concerned with the lack of specifically designed clothing for physically handicapped persons as a part of its long-term activities in the design, testing, and dissemination of information of self-help devices for the handicapped under a grant from the National Foundation.[1]

Definitive statistics are not available on the numbers of persons with varying types of physical disabilities who might profit from the availability of specially designed clothing. An approximation of the number, however, is indicated by the estimate that over 1,800,000 persons in the United States have suffered from strokes. The need for such clothing had made itself evident not only through the needs of the patients at the Institute of Physical Medicine and Rehabilitation but through numerous letters received regularly requesting information on the possible availability of such clothing.

Prior research by the staff of the Institute of Physical Medicine and Rehabilitation had shown that the clothing problems of physically handicapped persons centered around (1) design to permit greater ease in putting on and removing garments by individuals with limited muscle strength and limited range of motion in the various joints and by individuals who rely on braces, crutches, wheel chairs, and other mechanical aids; (2) design to permit greater social acceptance and increased self-esteem by severely disabled persons; (3) fabric choice to resist the undue wear caused by greater tension on the cloth as a result of the more strenuous physical activities required by certain disabled persons in dressing and undressing; undue wear caused by the friction of braces, crutches, wheel chairs, and other appliances and devices; and laundering and related care of clothing.

The results of the three-year research effort headed by Mrs. Cookman were first presented at a press showing in New York last October and then at another showing later that month before the

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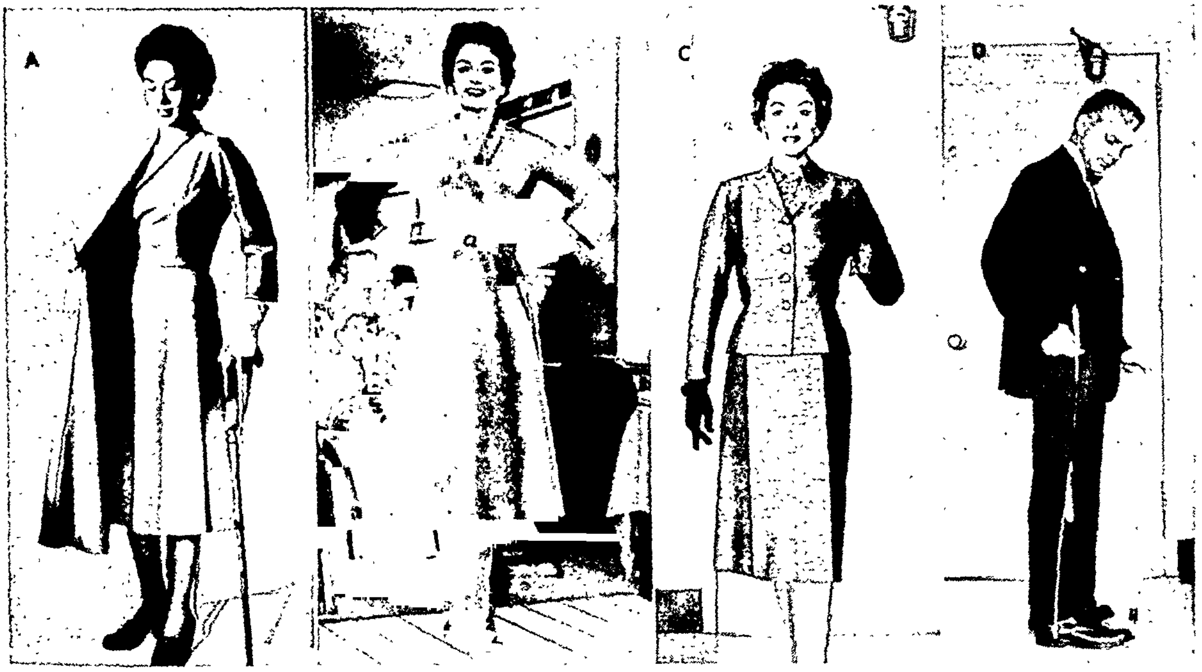
From the Department of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center.

annual meeting of the American Occupational Therapy Association. There were 17 models presented at these showings—tailored suits, slacks, blouses, dresses, dinner skirts, and gloves for women, and vests, shoes, ties, and suits for men.

Each of the models had been thoroughly trial-tested prior to manufacture. Testing based on function, utility, and fabric choice was conducted over a six-month period by disabled patients and staff members of the Institute of Physical Medicine and Rehabilitation, a number of whom wore each of the various models. Their suggestions were incorporated into redesigns, and then the redesigned models were tested.

Fabrics were chosen with deliberation after many months of checking with the Du Pont laboratories. They are mostly wash-and-wear nylons and Dacrons stitched with the strongest threads available, but care has been taken that the fibers do not generate too much electrostatic charge and will not cause wheel chair problems by sticking instead of sliding. Emphasis was also given to the use of closures which could be easily managed.



A, coat-dress, opened; *B*, coat-dress, closed; *C*, suit-dress; and *D*, man's slacks.

Currently six of the items in the collection have been produced by a new, nonprofit organization, Clothing Research, Inc., which is conducting a market test through the direct mail selling of these items. A large number of organizations contributed materials, skills, and time to the production of the current inventory of Clothing Research, Inc. Proceeds from the sale of these garments will be used for the further testing and development of new garments. Catalogs of the six items now available can be secured from Clothing Research, Inc., 307 W. 38th St., New York 1.

The Coat-Dress

Among the six items now available is the coat-dress (fig. 1 *A* and *B*). This garment was specially designed to counteract the destructive effect of crutch-walking on clothes—the pull across the shoulder blades and wear under the arms; to give greater ease in putting the garment on and taking it off; and to give greater comfort in wearing. The coat-dress is cut with extra width across the shoulders to provide more room for crutch-walking. Material is double under the arms at the side seams so that when the fabric wears from the crutches, the top fabric may be turned in for additional services from the fabric underneath.

The bodice is styled to hug the neck close and is cut wide across the chest so that crutch-walking motions will not pull it open. Sleeves are roomy enough to allow for well-developed arm muscles. The garment is buttonless and utilizes a single extra-large hook and bar closing at the waistline, thereby making dressing and undressing simple. The generous overlap of skirt insures that the dress will not come open, regardless of how active the wearer may be. The coat-dress is available in three colors in a range of sizes in crisp, crease-resistant fabric of 50% viscose rayon and 50% acrylic fiber (Acrilan).

The Suit-Dress

The currently available suit-dress (fig. 1*C*) is a classic, tailored garment with special features of value to crutch-users. These special features include inverted action pleats coming from the shoulder in front and a pleat at the center back allowing needed roominess for crutch-walking, for rising from chairs, and for getting in and out of an automobile. As with the coat-dress, fabric below the arms at the sides is double-thickness to withstand the rubbing action of crutches; when the top fabric wears through, it can be turned under a new, unworn piece of suit material. The jacket sleeves are made to allow for well-developed arm muscles.

The skirt has a heavy-duty, easy to reach, extra-long 12-in. zipper. The waistband closes with a new miracle fabric closure (Velcro). The wearer merely presses it shut and tiny nylon links mesh together to form a band that holds firmly but opens quickly and easily at a gentle tug.

The suit-dress is currently available in three colors in a range of sizes in a smartly slubbed menswear suiting fabric of year-around weight of 45% viscose rayon and 55% polyvester fiber (Dacron).

Other garments now available for women include slacks, a belt-pocket unit, and a wheel chair cape.

Men's Slacks

The only item currently available for men is slacks (fig. 1*D*), which have the following features: (1) two-way, heavy-duty, side-seam gripper zippers that open either top or bottom, and wide zipper facings that protect the leg and prevent zipper sliders from snagging underclothing; (2) button tab waistband fastenings and zipper fly front closing; (3) inside half belt that may be worn either toward front (for front drop) or toward back (for back drop) and that may be adjusted by changing button location on inside of waistband; (4) two front pockets with opening angled for easy access when sitting and two back pockets (one with button closing); (5) pleated fronts for comfort when sitting; (6) lined knees to protect pant legs from the abrasive action caused by knee locks of braces; (7) precuffed bottoms (when ordering, exact measurement of both waist and inseam must be given); (8) ample material in seat seam and at waist to allow for alteration if required; and (9) belt loops in matching fabric and color to be attached by wearer if he wishes to use a belt.

The men's slacks are available in two colors in a range of sizes in a medium-weight gabardine of 35% viscose rayon and 65% Dacron.

If the current market test indicates a sufficient market for the specialized line of "Functional Fashions for the Physically Handicapped," additional garments will be produced as the designs become available and will be distributed through normal commercial distribution channels.

In the meantime, while the market test is under way, research, development, and testing of new garments by the Institute of Physical Medicine and Rehabilitation will continue with the aid of a grant from the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare. It is hoped that the project will eventually be extended to cover all basic garments for children of all ages and winter outwear, rain wear, sleeping garments, underclothing, and other garments for handicapped men, women, and children.

400 E. 34th St. (16) (Dr. Rusk).

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SARCOIDOSIS AND THE KVEIM REACTION.—There is now evidence that sarcoidosis may be caused by an acid-fast spore, which is a pine-tree pollen. The occurrence of the disease predominantly in areas of pine-tree forests and among the rural residents of such areas, the recovery of the spore from patients and other findings recently reported indicate that the etiology of this disease may soon be known. The frequent difficulty in differentiating this disease from tuberculosis is not often overcome by the use of globulin determination, as the same change occurs in both diseases. Although the alpha fraction is often elevated along with the gamma globulin in tuberculosis and the gamma fraction is usually much more elevated in sarcoidosis, often recourse must be had to other laboratory means such as radiographic, bacteriologic and biopsy. The recently described Kveim test is said to be specific in the diagnosis of sarcoidosis. The Kveim reaction in sarcoidosis is a valuable diagnostic test. It is performed by the intracutaneous injection of a heated sarcoid lymph node or splenic suspension. If the test is positive, a violaceous papule appears at the site of inoculation within 3 weeks. It may reach a diameter of 5 to 10 mm. in 6 to 8 weeks. The lesion is similar histopathologically to sarcoidosis. The test is highly specific. Since it requires sarcoid material as a necessary ingredient, it is probably in the nature of an antigen-antibody reaction. In support of this are the following experimental findings: if gamma globulin from a sarcoidal patient or Kveim antigen is injected into a normal skin, only a mild reaction occurs; however, if they are mixed and then injected, a lesion similar to a typical sarcoid results.—P. G. Weil, M.D., Plasma Proteins, *American Practitioner and Digest of Treatment,* September, 1958.

DEPRESSANT ACTION OF LOCAL GASTRIC HYPOTHERMIA ON GASTRIC DIGESTION

USE IN CONTROL OF MASSIVE HEMATEMESIS

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The retardation of peptic digestion at low body temperatures first observed in vitro was found to be equally striking in vivo. Small animals, if sufficiently chilled and supplied with oxygen, were protected from digestion in the stomach of larger animals. This fact was applied in treating 19 patients who had unrelenting hemorrhages from the duodenum, stomach, and esophagus. A technique was evolved for circulating a coolant through a system of tubes and balloons in the stomach. The first experiences were encouraging, particularly in nine patients who had been bleeding profusely from duodenal ulcers and who ceased to bleed on cooling without recourse to operation. This therapy is rational for situations in which the digestive activity of gastric juice may be responsible for continued erosion and hemorrhage. It should not be relied on in situations complicated by blood dyscrasias, carcinoma, and other miscellaneous disorders.

William Beaumont and Alexis St. Martin more than a century ago wrote into the history of gastric physiology an immortal chapter on the nature of gastric digestion. Beaumont pursued relentlessly investigation of the digestive action of gastric juice on foods introduced into the stomach of Alexis St. Martin, a young French Canadian engaged in fur trading, who suffered a shotgun blast into his upper left abdomen and thorax which exposed the lung and tore a large rent in the anterior gastric wall. Beaumont managed the care of this mortal wound so skillfully that St. Martin, after a period of disability of three years, was restored to good health. Then began a series of observations interrupted by a period of four years in which Beaumont found it necessary to institute a search for the whereabouts of his unwilling subject who had absconded to Canada. These studies were commenced at Fort Mackinac Island, in the straits of Sault Sainte Marie, and continued, after St. Martin's long unannounced leave, at Fort Crawford in Prairie du Chien, Wis. All of Beaumont's experiments were done in military outposts of the United States Army; the final observations and experiments were performed in the city of Washington, and at Fort Niagara, N. Y. While his assignment was to look after the militia who aimed to preserve peace with the Indians in the areas of military outposts on the frontier, Beaumont found time to perform experiments on gastric secretion and digestion which excite our admiration today.

Beaumont's first publication was brief, recording three experiments performed in 1825. His epochmaking monograph summarizing his studies was published in 1833. Forty years after the appearance of this distinguished work, entitled "Observations on Gastric Digestion," there were still skeptics who were not convinced that the stomach secreted hydrochloric acid. In fact, Austin Flint Jr., who began his career as a physiologist in Buffalo, near where Beaumont performed his last observations on Alexis St. Martin in 1833, believed (1873) that the chief secretion of the stomach was lactic acid. He had been abetted in this belief by some observations Claude Bernard made in 1844, 11 years after the publication of Beaumont's monograph. Bernard's well-known experiments, in which the legs of frogs were submerged through a gastrostomy opening in the gastric juice of a dog's stomach, have served to mitigate the earlier serious error of Bernard's deductions concerning the nature of the acid in gastric juice.

Prior to Beaumont, it was generally believed, despite the observations of Réaumur (1752), Stevens (1777), Spallanzani (1785), and Young (1803), that gastric digestion was largely a triturative process, that it was the force of the gizzard in birds and of the gastric antrum in mammals which was largely responsible for the digestion of foods. Beaumont brought forth convincing evidence that gastric digestion was an active chemical process.

However, Beaumont failed to note the presence of an active enzyme in gastric juice. Schwann (1836), a pupil and colleague of Johannes Müller, boiled gastric juice and noted it had no digestive action on food. Schwann rightfully concluded there was an enzyme in gastric juice responsible for digestion, which he called pepsin. Wassman in 1839 elaborated on the observations of Schwann. The historic work of Rudolf Heidenhain (1870, 1878, 1883) of Wroclaw (Breslau), Poland, served to establish the presence of parietal (acid-secret-

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From the University of Minnesota Medical Center.
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ing) and chief cells (pepsin-secreting) in the stomach. It remained for Langley (1880-1882) to establish the presence of pepsinogen, the precursor of pepsin.

The linear relationship between enzyme action and temperature has long been known; that cold depresses peptic activity is known to every student of chemistry and biology. However, no special use has been made of this knowledge in the control of pepsin action in gastric digestion.

Assessment of Digestive Power of Gastric Juice

It is almost 20 years (1939) since gastric resection was first employed by one of us (O. H. W.) in the control of idiopathic esophageal stricture,[1] which it is perhaps now safe to label peptic stricture of the esophagus. It soon became apparent that this sensitivity of the esophagus to injury was owing to the circumstance that squamous epithelium does not resist digestion as well as the glandular epithelium of the stomach and upper reaches of the intestinal tract. These observations served to suggest perfusion of the cat's esophagus to assess the potential digestive action of gastric juice. For more than a decade in this clinic, the peptic activity of gastric juice has been determined by observing the damage done to the mucosa of the esophagus of the cat attending perfusion of the esophagus with gastric juice. It is noteworthy that perfusion with gastric juice obtained by overnight gastric aspirations of patients with duodenal ulcer quite regularly causes perforation of the cat's esophagus within a period of two hours when such juice is dripped into it.[2] Moreover, it is the pepsin that is responsible for this action. Hydrochloric acid in the range of the lowest pH levels that can be recovered from the stomach (0.1 *N*) fails to damage the esophageal mucosa noticeably on perfusion. Moreover, there appears to be no influence of temperature, within the physiological range, on the action of hydrochloric acid. When the gastric juice from a patient with duodenal ulcer is cooled and perfused through the esophagus of a cooled cat, the esophagus fails to exhibit evidence of esophagitis or perforation attending perfusion in the warm state (fig. 1).

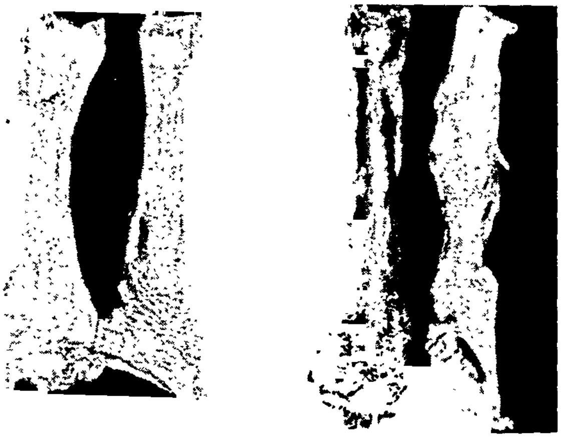

Fig. 1.—*Left*, esophagus of cat cooled to 25-30 C perfused with gastric juice cooled to 20 C obtained from patient with duodenal ulcer; results were 1+ to 2+, with little or no effect on esophagus. *Right*, esophagus of control cat at temperature of 37 C perfused with gastric juice at temperature of 37 C from patient with duodenal ulcer; results were 4+ to 5+, with severe esophagitis and perforation.

Effect of Systemic Hypothermia on Gastric Digestion—Fish and Small Animals

After completion of the observations just described, a study was undertaken of the influence of cold on gastric secretion and digestion, employing general and local hypothermia; observations were made on several animal species.[3] The desired levels of hypothermia were attained by reducing the environmental temperature in poikilothermic animals such as the fish, frog, toad, and snake and by brief immersion in ice water in small animals.

Two species of fish, trout (Salmo irideus) and catfish (Ameiurus nebulosus), were studied by measuring the rapidity of the digestion of a test minnow. Digestion of the minnow by a trout kept at 17 C was complete in 8 hours, but at 2 C, 17 hours were required to produce a similar result. The period of time required by catfish for complete digestion of the test minnow was somewhat longer, 16 hours at 20 C and 48 hours at 5 C. Only in fish have we encountered pepsin still active at 2 C.

Similar studies were carried out in frogs, small spring frogs being introduced manually into the stomach of large intact bullfrogs. Digestion of the small frogs in the stomachs of the bullfrogs kept at 26 C was essentially complete in 24 hours, whereas, when the temperature was maintained at 2 C, the spring frog was still alive after 11 hours (fig. 2), dead but intact at 24 hours, and only slightly digested at the end of a week. The digestion of decapitated and pithed frogs under similar circumstances produced equivalent degrees of digestion. The rate of digestion of spring frogs by toads differed only slightly from that reported for the bullfrog, being somewhat faster at 26 C and considerably slower at colder temperatures. The digestion of minnows by bullfrogs and toads maintained at 26 C was complete in 12 to 16 hours, while at 11 C little digestion had taken place after 72 hours.

The digestion of spring frogs by king snakes was also markedly slowed by hypothermia. At 33 C, tissue digestion was complete in 10 hours, while at 7 C, little digestion had occurred after 72 hours.

Studies of digestion in small mammals under general hypothermia were carried out with use of fasted white rats. They were first fed 2 Gm. of lean beef and then either immediately cooled to 20 to 25 C or kept normothermic. It was found that in six hours 98% of the meat was digested by the normothermic rat and only 2% was digested by the hypothermic animals.

Effect of Systemic Hypothermia on Gastric Digestion—Man and Dog

Technique of Achieving Local Gastric Cooling.—Local gastric hypothermia was achieved in man and the dog by circulating a cooling solution (equal parts ethyl alcohol and ice-cold water) through an intragastric balloon. Constant temperature and circulating volume were maintained by a hypothermia machine.

In Vivo Meat Bolus Digestion Studies.—In man, the rate of digestion of a 2-Gm. meat bolus contained in a wide-mesh, gauze sack was measured under normothermic and hypothermic conditions. The meat bolus was ingested by the subject and retained for four hours. It was then retrieved and a new bolus was swallowed and retained for an equal period. During the first four-hour period the intragastric balloon contained fluid at 38 C, while throughout the second four-hour period the cooling solution was circulated through the balloon to keep the stomach hypothermic. In human subjects, the mean weight loss of the bolus during the period of gastric cooling was 18%. In normothermic subjects, the mean weight loss of the bolus was 55%.

Data obtained from similar studies in dogs confirm these findings. The rate of digestion of a 2-Gm. meat bolus by gastric juice was studied in vitro at 37, 20, 11, and 5 C. Aliquots of juice were obtained from dogs with Heidenhain pouches after stimulation with meat, pilocarpine, and histamine. Specimens of unstimulated gastric juice were obtained from patients with duodenal ulcer and gastric ulcer and from those without gastric or duodenal lesions. Weight loss of the meat bolus at 37 C over a period of 10 to 21 hours was between 70 and 80%, while at 11 C the weight loss of the bolus was only 0 to 10%.

Influence of Local Cooling of Stomach on Volume of Gastric Secretion

The effect of hypothermia on the volume of gastric secretion was studied in human and canine subjects. In man, a no. 18 plastic nasogastric tube, connected to a continuous source of suction, was used to collect secretions; in the dog the pylorus was ligated and all secretions were collected by means of a gastrostomy tube. After placement of an intragastric balloon, gastric juice was collected for a two-hour period at normothermic temperatures; thereafter the stomach was cooled and hourly specimens were obtained during the ensuing four hours.

Interpretation of these data shows that the mean reduction in volume of gastric secretion after the initiation of hypothermia was 80% in man and 90% in the dog. Total free acid and total pepsin production were also markedly reduced.

Another experiment afforded lucid proof of the depressant effect of local gastric hypothermia on gastric digestion. An oxygen line, employing a polyethylene tube (no. 90), was fastened with a stitch to a small frog's nose. He was then immersed through a gastrostomy opening into a dog's stomach which was cooled to 4 C. When removed at 36 hours, the little frog, though at first inactive, was still alive and jumped as far as he ever did. His mate, who had been immersed in a warm dog's stomach, even though provided with an oxygen line, was well digested and died within a few hours (fig. 3).

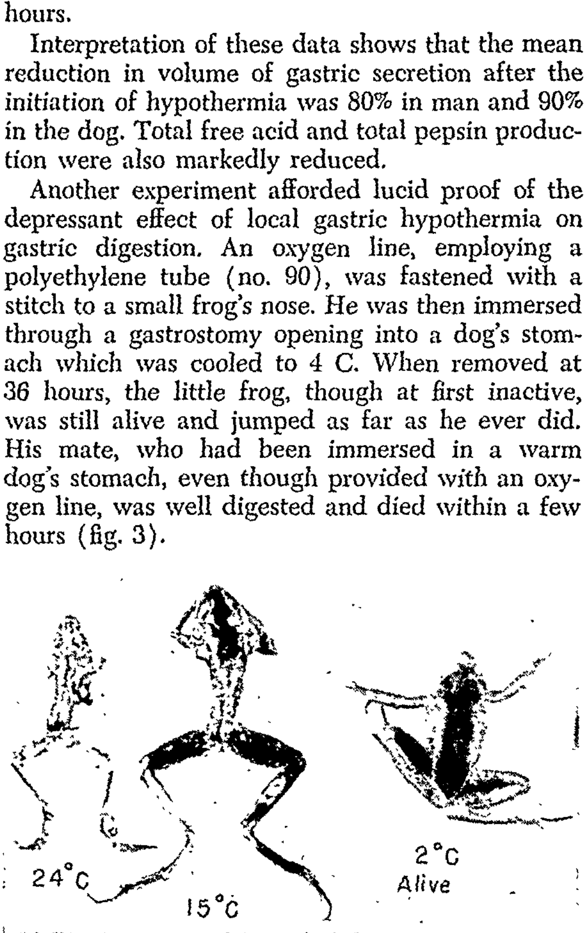

Fig. 2.—Digestion of three small spring frogs kept for six hours in stomachs of bullfrogs shows marked difference in degree. At 24 C spring frog was about 50% digested, at 15 C it was about 20% digested, and at 2 C frog was still alive. At 2 to 4 C small frogs have survived up to 20 hours within a bullfrog's stomach.

Technique of Local Gastric Hypothermia in Control of Massive Gastric Hemorrhage

The foregoing experiments suggested that control of massive gastric hemorrhage might be achieved by use of local gastric cooling.

In a study of the vital statistics of the ulcer problem in Minnesota, Casey[4] found that death from acute massive hemorrhage occurred in 42% of all patients who died from peptic ulcer in that state. In two-thirds of all deaths, hemorrhage played an important role. Emergency surgical treatment of massive upper gastrointestinal hemorrhage also carried with it a formidable mortality. The patients are usually in shock, with markedly reduced blood volumes. The additional stress of surgery is poorly tolerated by such patients. The site of bleeding is often unknown, thereby complicating and prolonging the surgery. The use of any agency which would make it possible to avoid surgery at such a time would be welcomed by everyone concerned.

Method of Cooling.—The machine now used (fig. 4) to induce gastric hypothermia has been greatly improved over the "homemade" model described in the original report.[3] This machine, while retaining the same basic components, has a number of distinct improvements. The circulation of fluid is constant, without the interruptions formerly necessary to balance inequalities of inflow and outflow. The cooling solution is now pumped out of as well as into the gastric balloon, thus permitting the use of a double-lumen tube of a much smaller over-all diameter. The advantages of automatic shut-off, should the balloon burst, are maintained.

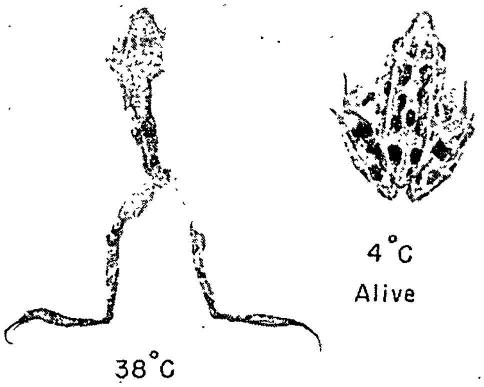

Fig. 3.—Protective effect of hypothermia. Both frogs were provided with an oxygen line by means of small polyethylene tube (*no.* 90). Frog on left was in normothermic (38 C) dog's stomach for six hours and underwent extensive digestion. Other frog was still alive after 36 hours in normothermic dog because dog's stomach was kept at 4 C by intragastric cooling balloon.

The temperature within the intragastric balloon is maintained at 10 to 14 C by an inflow of 150 to 200 ml. per minute at a temperature of 0 to —5 C. After the balloon has been passed into the patient's stomach, it is filled from a calibrated chamber so that it contains from 800 to 1,000 ml. After this, the fluid is circulated in an entirely closed system. Dial thermometers that register the temperature of the bath and the returning solution are mounted on the control panel, together with switches that control the pump and refrigeration unit. Supervision of the actively bleeding patient after initiation of gastric cooling requires participation of members from the clinical service and the cooling team, as well as nurses. As soon as bleeding appears to be controlled, further cooling may be safely conducted if a special duty nurse is at the bedside and a physician is nearby.

The machine has been in constant operation for periods up to 48 hours. During these runs the components have performed satisfactorily and in almost complete silence.

The Balloon and Its Clinical Use.—The intragastric balloon employed is one of the ordinary 10-cent rubber type, which will stretch to a capacity of about one liter. It is secured to the tubing by several turns of tightly wound 00 silk. The double-lumen tube to which the rubber balloon is attached consists of a no. 320 polyethylene inflow tube that is inserted through the side of the return tube, an 18 or 19 F. thin-walled plastic tube. The inner tube extends a centimeter beyond the end of the outer tube within the balloon. For the treatment of esophageal bleeding a 4-in. soft sheer latex balloon (condom) is attached to the tubing proximal to the gastric balloon. Two inches proximal to the gastric balloon attachment, the outer tube is constricted about the inner tube. Multiple holes bored in the outer tube both proximal and distal to the constricted point are covered by the esophageal balloon. Thus the circulating cold fluid returning from the gastric balloon is forced to flow through the esophageal balloon.

Clinical Safeguards During Cooling

Prior to the insertion of the balloon, the patient's stomach is completely evacuated of all clots by a nasogastric tube or by lavage with an Ewald tube, if deemed necessary. The patient's pharynx is then anesthetized with 5% solution of hexylcaine (Cyclaine) applied topically. Appropriate sedation is given to minimize restlessness and activity.

The empty balloon is wrapped about the end of the tubing, lubricated, and placed into the patient's mouth. The patient swallows this small bolus aided by light pressure on the tubing. Inflation of the balloon in the stomach unfolds the balloon and allows it to distend the stomach very slightly. The low temperature of the tubing minimizes the patient's discomfort. In the main, a tube in the nose is more easily tolerated by the patient than a tube in the mouth. This is an additional reason that we have reduced the diameter of the large tube initially used from 24 F. to a plastic tube corresponding in size to 18 F. In fact, for a child, a polyethylene tube no longer than 12 F. has been used.

A small nasogastric tube also is inserted beside the balloon into the stomach to evacuate blood as it appears and as an aid in evaluating continuance or cessation of bleeding. Frequent measurements of the blood pressure and occasional hemoglobin determinations also help in assessing the patient's response to local gastric cooling.

A constant-reading electronic thermometer registers the patient's temperature by means of an intrarectal thermocouple. The patient's systemic temperature usually remains normal, though external heat is quite regularly applied to insure maintenance of normal body temperature and for the patient's comfort. Mild sedation is continued as needed, and the nasogastric tube is irrigated frequently. The patient's vital signs are closely followed, and hemoglobin levels are measured every two hours. Transfusions of whole blood are continued until a normal hemoglobin level has been restored.

Despite the presence of the tubes, the alert, wide-awake patient is able to cough effectively and clear his throat of sputum and blood. In the aged, obese, or somnolent patient, regurgitation and aspiration into the tracheobronchial tree can be minimized by doing a prophylactic tracheotomy prior to intubation or soon after cooling is initiated. A semireclining position also helps to lessen the danger of tracheal aspiration. Even in the absence of frank regurgitation, stomach contents are often found in the oropharynx. In a few patients, after the start of gastric hypothermia, a few cubic centimeters of Congo red solution was put into the stomach through the nasogastric tube. The oropharynx was aspirated at regular intervals, and within 15 to 20 minutes Congo red could usually be demonstrated in the aspirated mucus of these patients. It therefore seems advisable to perform a tracheotomy early in all patients whose physical status is poor or wherever there is the slightest indication of a tendency to tracheal aspiration.

When the bleeding has stopped, as judged by the returns from the nasogastric tube and the patient's clinical status and hemoglobin values, cooling is continued only until a normal hemoglobin level is restored. Firm clot formation will usually have occurred in this period in the vessels previously bleeding, and a normal blood volume is restored, thus bringing the patient quickly to an optimal condition to withstand definitive surgical therapy should it prove necessary. The balloon is then deflated and removed. Close observation of the patient is continued, and the further management of the situation can be planned under more favorable circumstances.

Prolonged cooling of the stomach has been carried out in anesthetized animals for 48 hours and in man, up to 125 hours, without any apparent damage to the stomach or to general well-being of the subject. In well over 200 episodes of local gastric cooling on dogs and man the balloons and tubing have functioned satisfactorily without evidence of leaks or obstruction. To maintain the highest degree of safety, balloons and tubing are used only once in clinical cases.

Results of Local Gastric Hypothermia

To the present time, 19 patients with massive unrelenting upper gastrointestinal hemorrhage have been treated by the technique of local gastric hypothermia. In many instances large quantities of blood had been administered prior to the initiation of cooling. Moreover, the majority of these patients were in shock despite rapid transfusion, and hence were in a condition too precarious for emergency operation.

The patients were divided into four major categories according to bleeding site and etiology: (1) duodenum, (2) stomach, (3) esophagus, and (4) miscellaneous.

The results of treatment are as follows (see table):

Duodenal Ulcer.—Nine patients were bleeding from duodenal ulcer. At the institution of gastric cooling, six of the patients were in shock; the mean hemoglobin value was 8.5 Gm. per 100 cc., and an average of 5 units of blood had been infused. Gastric cooling was employed for an average of 15.7 hours. Prompt cessation of hemorrhage occurred in all patients.

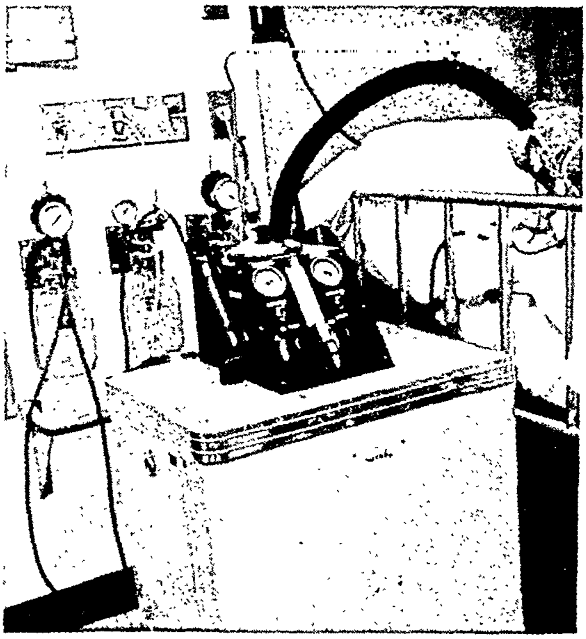

Fig. 4.—Hypothermia machine. Temperature of 10 to 14 C is maintained by pumping in mixture of ethyl alcohol and ice water at —5 to 0 C. Gauges on control panel register temperature.

The coagulation mechanisms in these patients were normal as measured by bleeding, clotting, and prothrombin times. Platelet counts were normal. It was noted that the bleeding stopped in the majority of the cases within three to four hours, as judged by the appearance of decreasing amounts of blood from the nasogastric suction. However, cooling was continued until the hemoglobin levels were returned to normal.

Gastric Ulcer.—There is only one patient with gastric ulcer. This patient, an 80-year-old female with sudden massive hematemesis, was in shock despite a transfusion of 1,000 cc. of blood. Her hemoglobin level was 8.7 Gm. per 100 cc., and her coagulation mechanisms were normal prior to local gastric hypothermia. Her bleeding stopped soon after initiation of gastric cooling, and a hemoglobin value of 13 Gm. was restored after 20 hours of treatment. No further bleeding occurred.

Esophageal Bleeding.—Three patients with massive hemorrhage from esophageal varices were treated a total of four times. Local gastric and lower esophageal cooling were achieved by the addition of a thin 4-in. latex esophageal balloon proximal to the gastric balloon, as described previously. At the onset of cooling, all of these patients were in shock and had been given an average of 6 units of blood. The mean hemoglobin level was 8 Gm. per 100 cc. Each patient had undergone unsuccessful trials with esophageal tamponade by means of the Sengstaken-Blakemore technique.

Results of Local Gastric Hypothermia in Nineteen Patients with Massive Hematemesis

			Hypothermic Course					Results		
								Operation Necessary		
Lesion	No. of Patients	No. of Times Cooled	Ml. of Blood Prior to Cooling	Coagulation Mechanisms	Shock	Cooling Time, Hr.	Status of Bleeding	For Control of Bleeding	Delayed, When Condition Stable	No Further Therapy
Duodenal ulcer	9	9			6			0	1	8
Mean			2,500	All		15.7	Ceased in			
Range			500-6,000	normal		5-25	all cases			
Gastric ulcer	1	1	1,000	Normal	1	20.0	Ceased	0	0	1
Esophageal varices										
Intrahepatic obstruction	2	2	1,000 1,000	Abnormal	2	125.0 7.0	Ceased Slowed	1	0	1
Extrahepatic obstruction	1	2	4,500 5,000	Normal	2	17.0 26.0	Ceased	0	1	0
Miscellaneous cases										
Gastric cancer with thrombocytopenia	1	1	9,500	Abnormal	0	24.0	Ceased	0	0	1*
Metastatic cancer (breast) with steroid-induced gastric ulcer	1	1	3,500	Abnormal	1	7.5	Slowed	0	0	1*
Stress-induced duodenal ulcer	1	2	1,000 1,000	Normal	0	28.0 48.0	Ceased	0	0	1
Postoperative bleeding with coagulation defects	2	2	5,500 4,500	Abnormal	2	6.0 22.0	Slowed Slowed	0 1	0 0	1* 1
Gastric erosion with uremia	1	2	4,800 750	Abnormal	1	6.0 13.0	Ceased	0	0	1
Totals	19	22			15			2	2	15

* Patient died before more definitive therapy could be instituted.

Intrahepatic Block (Cirrhosis): The first patient, a 55-year-old alcoholic with severe Laennec's cirrhosis, was bleeding massively from esophageal varices. His hemoglobin level prior to cooling was 11 Gm. per 100 cc. He was treated for five days, with satisfactory control of his bleeding. His hemoglobin value remained normal over this entire period, but he died from liver failure.

The second patient, also with far-advanced alcoholic cirrhosis, was admitted in shock with a hemoglobin level of 8.4 Gm. per 100 cc. Local gastric hypothermia was carried out for seven hours. Although his bleeding was slowed, it was decided to perform transesophageal ligation of his varices. His hemoglobin value at the time of surgery was 13 Gm.

Extrahepatic Block: A 21-year-old girl with congestive splenomegaly (Banti's disease) due to cavernomatous transformation of the portal vein had massive hematemesis with shock on two separate occasions. The massive hemorrhage was successfully arrested on each occasion by local cooling. She later underwent successful definitive surgical treatment.

These observations would suggest that local gastric cooling should be invoked immediately for the control of hemorrhage from the bleeding esophageal varices of portal hypertension. The observed efficacy of local gastric cooling in the control of the hemorrhage of portal hypertension lends some credence to an earlier thesis that bleeding from esophageal varices was in large measure acid-peptic in nature.[5]

Miscellaneous.—The patients in this group were bleeding from the stomach or duodenum, but unusual circumstances attended the hemorrhagic episodes. These factors were abnormal clotting mechanisms, previous steroid therapy, carcinoma, complications of surgery, and stress.

Carcinoma with Abnormal Clotting Mechanisms: Two patients had disseminated metastatic carcinoma with marked thrombocytopenia, elevated prothrombin times, and prolonged bleeding and clotting times. One patient was bleeding from a gastric carcinoma and the other from a steroid-induced gastric ulcer. Although bleeding in these patients was temporarily controlled, they were not candidates for definitive surgery and recurrent bleeding attended their terminal period.

Stress Ulcer: The stress associated with cervical fracture and resultant quadriplegia evoked massive hemorrhage in a 16-year-old boy on two separate occasions. A marked drop in hemoglobin value, massive hematemesis, and melena characterized these episodes. His bleeding promptly stopped on both occasions after the initiation of local gastric hypothermia.

Bleeding in the Patient After Operation: Two patients bled massively during complicated, prolonged postoperative courses. Both patients were in shock and had received between 8 and 10 units of whole blood replacement prior to cooling. The bleeding in one patient with a platelet count of 18,000 per cubic millimeter and a prolonged bleeding time was slowed. However, she continued to require some blood replacement and therefore operative treatment was elected while her blood volume was near normal.

The other patient had multiple ulcerations of his stomach, duodenum, and esophagus. The hemorrhage was slowed by local gastric hypothermia, but the unrecognized presence of a large firm rubbery clot in the stomach prevented efficient cooling. When the patient died unexpectedly six hours later, the hemoglobin level was 14.6 Gm. per 100 cc. This experience has taught the necessity of evacuating all clots from the stomach prior to the introduction of the cooling balloon.

Gastric Erosion with Uremia: A 13-year-old girl with chronic renal disease, thrombocytopenia, and hypoprothrombinemia had a massive gastrointestinal hemorrhage requiring replacement of 4,000 cc. of blood prior to initiation of local gastric hypothermia. The patient was in shock, with a hemoglobin level of 10 Gm. per 100 cc. Local gastric cooling produced prompt cessation of bleeding, and her vital signs and hemoglobin value stabilized in six hours. Three days later bleeding recurred to a lesser degree; it again was rapidly controlled with use of the same technique. (This patient has recently undergone successfully surgical management of urinary obstruction.)

Comment

The hazard of undertaking emergency operative measures to control hemorrhage is avoided by the employment of gastric cooling, by permitting restoration of blood volume, and by subsequent study to determine the site of bleeding and preparation for future definitive therapy. The experience with this group of cases has been a rewarding one, which has suggested definitely that depression of gastric secretion and peptic activity by local gastric cooling is of merit in the management of massive upper gastrointestinal hemorrhage.

Gastric hypothermia would not appear to be a promising method for the treatment of gastric or juxtagastric bleeding in association with metastatic carcinoma and allied disorders accompanied by low platelet counts and elevated prothrombin times. Similarly, in many postoperative states, attended by gastric hemorrhage and manifestations of deranged clotting mechanisms, local gastric hypothermia cannot be expected to elicit the same dramatic therapeutic responses as occur in peptic ulcer hemorrhage. Moreover, the terminal condition of the patients in this latter category frequently tips the scales in the direction of an unfavorable result. Nevertheless, cessation of bleeding has been achieved in a few patients in this group. A larger series of cases will be required to evaluate the usefulness of hypothermia in the control of esophageal hemorrhage.

Our small experience with local gastric hypothermia is encouraging. The method will need a longer trial in our and other hands to evaluate more precisely its advantages and shortcomings. In hemorrhage from peptic ulcer syndromes, an accurate diagnosis as to the exact site of hemorrhage apparently is not so important, whether it concerns a duodenal or gastric ulcer or hemorrhage from bleeding esophageal varices, though obviously it would be good to have precise information, if possible. Our own limited experience with hemorrhagic dyscrasias, with aberrations in the components essential to the clotting of blood, would suggest that recognition of such abnormalities is important, so that awareness of the need of invoking other therapeutic agencies may be prompt.

Summary

Gastric digestion is retarded considerably by local gastric cooling. With this procedure, a striking decrease in the volume of gastric secretion occurs. Inhibition of peptic activity is the primary cause of the suppression of gastric digestion. Observations with use of systemic cooling were made on the fish, frog, toad, and rat, and observations with local gastric cooling were made in dog and man. Only in fish have we encountered a gastric pepsin fairly active at 2 C. Even so, however, there is a notable retardation of gastric digestion attending systemic cooling in fish (trout and catfish).

Gastric hypothermia inhibits digestion of an intact frog placed in the stomach of a large bullfrog or in the stomach of a dog. In the warm animal, death and digestion of the inhabitant is a rapid and usual sequence. In the cool state, neither digestion nor death occur!

Local gastric cooling has been employed as a therapeutic adjunct in the management of massive gastric hemorrhage. Nine patients with massive hematemesis from actively bleeding duodenal ulcers have been cooled successfully, with cessation of hemorrhage and without recourse to operation. A similar result attended use of local gastric cooling in a patient with massive hemorrhage from a gastric ulcer. Three patients with portal hypertension and massive hemorrhage have been cooled. Cessation of bleeding occurred in two of these and was slowed in the other.

The method has also been used in miscellaneous conditions causing massive hematemesis, including (1) gastric and breast cancers with thrombocytopenia, (2) gastric erosions occasioned by uremia, (3) steroid ulcers with ensuant hemorrhage, and (4)

severe gastric hemorrhage in early convalescence from other surgical procedures. The results in this group have been variable—in some instances, disappointing. In others there has been slowing or cessation of the gastric hemorrhage. Obviously, these conditions do not constitute the best indications for use of local gastric hypothermia in the control of hemorrhage.

These observations suggest definitely that local gastric cooling is of promising therapeutic value in the management of massive hematemesis from peptic-ulcer-linked conditions of the duodenum, stomach, and esophagus.

Addendum

Since this paper was presented, nine additional patients have been subjected to local gastric hypothermia for massive gastric hemorrhage. Two patients had bleeding esophageal varices; the bleeding was controlled and successful definitive surgical therapy was carried out. There were three patients with severe hemorrhage from diffuse gastritis which was successfully controlled; surgical correction was done after adequate blood replacement and supportive therapy. There were two patients with postoperative bleeding which was successfully controlled. One of these, who entered the hospital with a blown-out duodenal stump, a gastric-cutaneous fistula, and complete obstruction of both afferent and efferent jejunal loops, ultimately died from peritoneal sepsis. A 4-year-old boy, treated intensively with cortisone for rheumatic fever for six weeks, bled massively twice from a steroid-induced duodenal ulcer. The first episode was quickly controlled. Owing to parental restraint and reluctance to have either local gastric cooling or surgery instituted for the second episode, only a futile last-resort attempt could be made to try to control the hemorrhage when it recurred. Bleeding was also successfully controlled in an 82-year-old woman with massive bleeding from an antral gastric ulcer, which proved, on operation, to be benign.

412 Union St. S. E. (14) (Dr. Wangensteen).

The hypothermia machine used is made by the Swenko Manufacturing Company, Minneapolis.

Just where in Washington Beaumont did his experiments on Alexis St. Martin is not known. We believe they were done at the northeast corner of 10th and E streets, N. W. If anyone has definite knowledge regarding this point, we would appreciate his sending us any information, letters or documents, giving evidence on this matter.

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THE POSTMENOPAUSAL OVARY.—Urinary estrogen and gonadotropin excretion was determined in 51 normal postmenopausal women, 45 to 81 years of age, and in 30 surgically castrated women, 23 to 52 years of age. In the postmenopausal women the menses had ceased from one to thirty-three years previously. Urinary estrogen excretion of the postmenopausal women was approximately twice that of the castrated women. Although there was overlapping, the difference between the values for the 2 groups was highly significant. Estrogen excretion remained constant throughout the postmenopausal years, being the same sixteen to thirty-three years after the menopause as one to five years thereafter. Urinary gonadotropin excretion was elevated in each of the postmenopausal and castrated women. The average value for the ovariectomized women was significantly higher than the average for the postmenopausal women. Urinary gonadotropin excretion of the postmenopausal women showed no tendency to decrease with advancing years. Two postmenopausal women who received hog pituitary FSH responded with increased urinary excretion of estrogen and amelioration of menopausal symptoms. The other 4 postmenopausal women and the 2 castrated patients who received pituitary FSH did not respond. It is concluded that the postmenopausal ovary retains a small but significant secretory function and that it is the major source of postmenopausal production of estrogen.—C. A. Paulsen, M.D.; R. B. Leach, M.D.; H. Sandberg, M.D.; S. Sheinfeld, M.T.; and W. O. Maddock, M.D., Ph.D., Function of the Postmenopausal Ovary. Comparison of Urinary Estrogen and Gonadotropin Excretion and Response to Administration of FSH in Postmenopausal and Ovariectomized Women, *Journal of the American Geriatrics Society*, November, 1958.

THERAPY OF HYPERTENSION WITH ORALLY GIVEN SYROSINGOPINE

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Syrosingopine, a drug derived from reserpine, was administered orally to 77 ambulant patients for the treatment of essential hypertension. Group 1 consisted of 38 patients not previously treated for hypertension. Group 2 consisted of 34 patients who had been maintained on therapy with reserpine, were changed to therapy with syrosingopine, and were maintained on it for an average of three months. Group 3 consisted of five patients on combination drug therapy who had severe mental depression or other symptoms of intolerance when maintained on therapy with older antihypertensive drugs. In group 1, 16 patients (42%) responded with a clinically significant fall in mean blood pressure. In group 2 the blood pressure was controlled without side-effects by individual adjustment of dosage. In group 3 the dosage used (3 mg. of syrosingopine per day) maintained the desired antihypertensive effect without nightmares, nasal congestion, or other significant side-effects.

The effectiveness of Rauwolfia and its derivatives in the therapy of hypertension has been well demonstrated in many studies.[1] In many patients with mild to moderate hypertension, such preparations in appropriate dosage reduce the mean blood pressure 20 mm. Hg or more, and in some the blood pressure may return to normal. In other patients, usually with more marked blood pressure elevations, the Rauwolfia preparations play a useful role in combination drug therapy. The need for continuous therapy is obvious, and tolerance to the preparations after long administration has not been observed.

The limiting factor in the widespread use of Rauwolfia preparations has been the disturbing side-effects. The frequency and severity of these depend on the dosage being used. However, in the dosage range for therapeutic effect, over half of the patients have been noted to complain of such symptoms as drowsiness, terrifying nightmares, depression, nasal congestion, abdominal cramps, gastrointestinal bleeding, fatigue, weakness, dysuria, and impotence.[1b] Fortunately, only a rather small percentage of patients have experienced symptoms so severe that the drug had to be withdrawn, but such ancillary effects may make Rauwolfia therapy unsuitable for long-term administration.[2] Pharmaceutical chemists have been vigorously searching for Rauwolfia derivatives which exhibit less of these undesirable side-effects while retaining antihypertensive potency.

Syrosingopine or carbethoxysyringoyl methylreserpate (Singoserp) is one of the most recently produced synthetic compounds derived from reserpine. It was prepared in the hope of removing the undesirable attributes of the naturally occurring drugs of this class. It has been experimentally shown to be a nontoxic yet active antihypertensive agent in several species of animals, with considerably fewer sedative and gastrointestinal effects than reserpine.[3] Darvill[4] found syrosingopine to be an effective hypotensive agent in clinical studies in 28 patients, practically none of whom experienced significant side-effects.

Methods and Results of Present Study

Over the past nine months, we have studied the effects of syrosingopine administered orally to 77 ambulant patients with essential hypertension at the University of Texas Medical Branch. Patients were generally seen at intervals of twice weekly for two to three weeks for the establishment of baseline levels of blood pressure. The drug was administered in divided doses two to four times daily. At each visit throughout the study, careful clinical evaluation of each patient was made, including repeated blood pressure determinations, usually made while the patient was sitting and after a rest period of one hour. Careful inquiry was made as to possible side-effects. Laboratory studies, such as periodic electrocardiograms, blood cell counts, urinalyses, and blood urea nitrogen level determinations were made on all patients, usually at intervals of two to three weeks. The patients were divided into three groups for purposes of the study.

Group 1.—Group 1 included all patients who had not previously been treated with an antihypertensive agent and who were given syrosingopine as the first such medicament. There were 38 patients with essential hypertension admitted to the cardiovascular clinic on no medication, including 27 females and 11 males. All of the patients were Ne-

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groes except four. Syrosingopine was administered to them in varying dosage. There was an initial control period of at least three to four visits, during which base-line blood pressures were established. Administration of the drug was generally begun at a dosage of 0.25 mg. given four times daily, and at times this was increased at intervals of two weeks to a maximum of 1 mg. four times daily. During this time no additional medicaments were prescribed. The duration of therapy was two to five months, with an average of three months.

TABLE 1.—*Blood Pressure, in Millimeters of Mercury, in Patients in Group 1 Before and During Therapy with Syrosingopine*

Case, No.	Av. Before Therapy	Av. During Therapy, Mg. per Day: 1 (24 Patients)	2 (11 Patients)	3 (11 Patients)	4 (6 Patients)	Maximum Reduction*	Change in Mean Blood Pressure
1	187/110	...	171/112	...	...	—16/+2	—4
2	186/106	184/98	...	...	...	—2/—8	—6
3	240/130	245/116	...	...	...	+5/—14	—8
4	280/146	200/125	...	...	...	—80/—21	—40
5	179/115	176/112	...	...	...	—3/—3	—3
6	197/120	150/103	...	...	...	—47/—17	—27
7	252/145	168/117	...	...	...	—84/—28	—47
8	168/112	160/100	...	...	...	—8/—12	—11
9	188/120	168/117	...	...	...	—20/—3	—9
10	175/112	192/104	140/97	...	...	—35/—15	—22
11	194/104	170/105	113/100	...	..	—81/—4	—30
12	263/141	...	...	...	250/140	—13/—1	—5
13	195/110	...	...	..	140/70	—55/—40	—45
14	207/127	152/102	170/115	186/124	...	—55/—25	—35
15	180/104	180/105	...	...	...	0/+1	+1
16	201/109	...	160/79	...	...	—41/—30	—34
17	215/110	230/118	...	...	208/100	—7/—10	—9
18	239/142	210/110	210/130	245/130	...	—29/—32	—31
19	186/114	153/103	185/100	157/97	140/80	—46/—34	—38
20	148/114	...	...	167/104	160/100	+12/—14	—5
21	206/116	...	166/104	...	...	—40/—12	—21
22	190/125	...	...	177/120	...	—13/—5	—8
23	224/134	200/132	...	220/130	220/130	—24/—2	—9
24	191/100	175/92	...	175/96	...	—16/—8	—11
25	170/113	174/118	...	...	...	+4/+5	+5
26	207/98	206/100	...	...	...	—1/+2	+2
27	163/101	165/72	...	...	...	+2/—29	—19
28	183/113	...	173/106	...	...	—10/—7	—8
29	210/103	190/102	...	...	...	—20/—1	—7
30	185/116	...	217/118	...	...	+32/+2	+12
31	192/96	...	...	182/85	...	—10/—11	—11
32	261/152	...	...	176/120	...	—85/—32	—50
33	171/119	...	...	185/108	...	+14/—11	—3
34	233/127	200/117	...	...	...	—33/—10	—18
35	160/91	130/87	...	...	...	—30/—4	—13
36	218/116	...	180/92	...	...	—38/—24	—29
37	150/110	...	...	168/97	...	+18/—13	—3
38	170/104	150/97	...	...	...	—20/—7	—11

* Average blood pressure reduction was —23/—12.5.

Table 1 lists the average of the blood pressures during the control period and the period when patients were on various dosage regimens with syrosingopine. There were 11 patients with diastolic blood pressure levels from 91 to 109, 16 with 110 to 119, and 11 with 120 mm. Hg or greater. Six of these patients had an initial blood urea nitrogen level of 25 to 87 mg.%, and these values remained essentially unchanged during the period of therapy.

The average blood pressure for this entire group decreased from a control value of 199.1/116.5 to 176.1/104.0 mm. Hg on the various dosage schedules. The reduction in the mean blood pressure (diastolic pressure plus one-third of pulse pressure) after therapy exceeded 20 mm. Hg in 13 patients, and the diastolic pressure returned to normal in an additional 3, making a total of 16 patients (42%) with significant clinical response. In five patients the diastolic pressure was reduced below 90 mm. Hg. The most dramatic response appeared to occur in the patients with severe essential hypertension with diastolic pressures initially over 120 mm. Hg. Six of 11 such patients showed a drop averaging 38.3 mm. Hg in mean pressure.

In individual patients, it was not possible to correlate a decreasing blood pressure with increasing doses of the drug. In two patients (cases 14 and 18), a satisfactory initial response was followed by an increase in blood pressure despite larger doses of syrosingopine. However, the blood pressures did not rise to the original control levels. This refractoriness may have been due to the progression of their arteriolar disease. Four of the 14 patients on the higher dosage levels of 3 and 4 mg. per day showed significant drops in mean blood pressure (over 20 mm. Hg), or a fall in diastolic pressure to below 90 mm. Hg. Six of 11 patients on the 2 mg. per day regimen showed significant declines in the mean blood pressure. Seven of 24 patients showed significant falls in blood pressure on the lower dosage schedule of 1 mg. per day.

Group 2.—Group 2 consisted of patients with essential hypertension treated with reserpine whose response was studied after change of medicament to syrosingopine. There were 34 patients who had been maintained on reserpine therapy alone for periods of 1 to 12 months in whom syrosingopine in varying dosages was substituted for the older drug. No other change in medicament was made during this period of observation. In a number of patients, syrosingopine was given in gradually increasing doses, with increases being made at two-week intervals. Recorded blood pressures were discarded for the first two weeks after cessation of reserpine therapy in order to avoid residual reserpine effects. Follow-up studies on patients on syrosingopine therapy were done for one to nine months (average three months).

Table 2 summarizes the therapeutic results observed in this group. The average blood pressure determination is given for each patient at various dosage levels of reserpine therapy. The right half of the table lists the average changes in blood pressure during treatment with various doses of syrosingopine. The average change on the dose of 1 mg. per day of syrosingopine in 24 patients was an increase in pressure of 0.1 mm. Hg systolic and 0.9 diastolic. There were three patients (cases 59, 65, and 70) with increases in mean pressures greater than 20 mm. Hg after being changed to 1 mg. per day of syrosingopine from previous reserpine dosages of 1 mg. per day in two patients and 0.5 mg. per day in one. One (case 40) showed a temporary decrease in mean arterial pressure of 20 mm. Hg. On the syrosingopine dosage of 2 mg. per day, 12 of these patients had an average increase in blood pressure of 2.3/1.0 mm. Hg. One patient (case 46) showed a significant increase of 32 mm. Hg in mean blood pressure, while another (case 69) showed a significant decrease of 27 mm. Hg in mean blood pressure. In six of these patients who received 3 mg. per day of syrosingopine, there was an increase in average blood pressure of 5.3/0.4 mm. Hg. One of these patients (case 59) had a significant increase of mean blood pressure of 22 mm. Hg. On the syrosingopine dosage of 4 mg. per day in six patients, there was an average decrease in systolic pressure of 1.7 mm. Hg and decrease in diastolic pressure of 3.7 mm. Hg. One patient (case 59) had a significant increase in mean blood pressure of 22 mm. Hg; two others (cases 49 and 61) had significant decreases of mean blood pressure of 31 and 21 mm. Hg.

TABLE 2.—*Blood Pressure, in Millimeters of Mercury, in Patients in Group 2 During Therapy with Reserpine and Syrosingopine*

	Av. on Reserpine, Mg. per Day			Av. Change on Syrosingopine, Mg. per Day			
Case No.	0.5 (11 Patients)	0.75 (4 Patients)	1.0 (19 Patients)	1 (24 Patients)	2 (12 Patients)	3 (8 Patients)	4 (6 Patients)
39	205/110	...	...	−12/+8	...	...	...
40	...	...	234/128	−24/−18	−24/+2	+11/+2	...
41	...	...	180/123	...	...	−3/−3	...
42	...	...	167/122	...	...	...	0/−1
43	...	169/102	...	...	+24/−2	...	...
44	...	...	227/125	...	−10/−7	...	...
45	...	...	166/102	−6/+4	−14/−4	...	...
46	157/100	...	...	+8/−28	+60/+18	...	...
47	137/99	...	...	+33/+6	+36/+1	...	...
48	190/102	...	...	0/0	...	...	...
49	177/108	...	...	−24/−7	+8/−8	−20/−11	−37/−28
50	...	...	171/111	−18/−8	...	...	...
51	...	...	171/118	−2/−16	...	...	...
52	166/84	...	...	...	...	...	+16/+4
53	179/105	...	...	...	−6/+1	...	...
54	...	...	227/123	+33/+7	...	...	...
55	...	...	146/102	...	...	+21/+2	+14/−2
56	...	...	190/110	−14/−16	...	−15/−14	...
57	...	...	182/116	+18/+1	...	...	...
58	...	165/115	...	...	...	−1/0	...
59	200/105	...	...	0/+27	...	+20/+25	+20/+25
60	...	...	145/86	+2/+8	...	...	...
61	...	231/128	...	−1/−10	...	...	−23/−20
62	...	...	160/80	...	0/−1	...	...
63	...	...	160/100	...	+15/+8	...	...
64	...	...	260/112	−15/+4	...	...	...
65	...	...	166/106	+34/+19	...	...	...
66	...	...	175/106	−25/−3	...	...	...
67	175/109	...	...	−7/+8	...	...	...
68	...	180/110	...	0/0	...	...	...
69	178/108	...	...	−8/−3	−65/−8	...	...
70	...	...	140/70	+45/+45	...	...	...
71	...	...	167/103	−15/−1	+3/+12	+34/+2	...
72	180/105	...	...	0/−5	...	...	...
Av.	176.73/103.18	186.25/113.75	180.89/107.52	+0.1/+0.9	+2.3/+1.0	+5.3/+0.4	−1.7/−3.7

Group 3.—Group 3 consisted of patients with severe essential hypertension on combination drug therapy who were conspicuously intolerant of Rauwolfia products. Five patients with severe hypertension on multiple antihypertensive therapy (Rauwolfia, chlorothiazide, hydralazine, and ganglionic blocking agents) were unable to continue an effective regimen because of severe intolerance to the older alkaloids. The symptoms consisted of severe mental depression in two patients and nasal congestion in three. In these five patients, attempts were made to change from one to another of the various Rauwolfia preparations (the crude derivative, reserpine, rescinnamine, and alseroxylon), but no such changes proved effective in lessening the side-effects. When Rauwolfia derivatives were deleted from the therapy, there was clearing of the side-effects but the blood pressure rose. Syrosingopine therapy in doses of 3 mg. per day was substituted for the previous Rauwolfia agents in these five patients, with as effective antihypertensive action as on the previous regimen and without significant side-effects.

Side-effects

In addition to the cases described in group 3, above, there were nine patients in group 2 who had experienced severe side-effects related to reserpine therapy. These consisted of severe and distressing nasal congestion in eight, with abdominal cramps and loose stools in one of these, and nightmares in one additional patient. The reserpine dosage on which these symptoms developed was 1 mg. per day in six and 0.5 mg. per day in three. Therapy in these patients was changed to that with syrosingopine in doses increasing to the point at which follow-up blood pressure determinations were essentially similar to those during reserpine therapy. The dosage of syrosingopine required to accomplish this was 1 mg. per day in three patients, 2 mg. per day in two, 3 mg. per day in two, and 4 mg. per day in two. Side-effects persisted in only three of these patients receiving dosages of syrosingopine of 2, 3, and 4 mg. per day. Nasal congestion persisted in one patient, nightmares in another, and abdominal cramps with nasal congestion in a third. In the latter patient, the symptoms of drug intolerance disappeared when the syrosingopine dosage was reduced from 2 mg. to 0.5 mg. per day, while the previous effective blood pressure reduction was maintained at the lower dosage.

No patients developed side-reactions with syrosingopine who had previously tolerated reserpine. Of the 38 patients in group 1, who did not receive reserpine, only one (case 4) developed a side-effect from syrosingopine. This consisted of nightmares which occurred when dosage of 1 mg. per day was given. There was good reduction of blood pressure in this instance, and therapy did not have to be discontinued as the side-effect was easily tolerated.

Pulse rates before and after the administration of syrosingopine showed no constant change, although there was considerable variation in individual patients over the time they were observed. The prominent bradycardia usually accompanying reserpine therapy was not seen. The drug appeared to produce little or no effect on the alertness of the patients, and there was no definite tendency to develop drowsiness or depression. Follow-up observations on blood cell counts and urinalyses in our patients showed no toxic hematological or renal effects. No gastrointestinal symptoms were noted except in the one patient previously discussed, who developed abdominal cramping on both reserpine and syrosingopine therapy. There was no instance of gastrointestinal bleeding.

Comment

It would appear from our studies in previously untreated hypertensive patients that syrosingopine is moderately effective as an antihypertensive drug. A significant blood pressure reduction was obtained in 16 (42%) of the patients treated with this drug alone, and in 5 of these the diastolic pressure was reduced to normal levels. These figures are roughly comparable to those observed with other types of Rauwolfia therapy. In general, patients who had been treated with reserpine could be given syrosingopine with maintenance of similar blood pressure reduction. The required dosage of syrosingopine appears to be higher than that of reserpine, but the drug is well tolerated in all dosage ranges tested.

The chief advantage of syrosingopine over other Rauwolfia derivatives seems to us to be the relative infrequency with which it produces disturbing side-effects. In our entire group of 77 patients, 14 of whom were markedly intolerant to one or several of the older Rauwolfia preparations, we observed side-effects due to syrosingopine in only four. In many hypertensive patients, the psychic and bradycardic effects of the established alkaloids may be desired; in such patients those drugs would still seem to be indicated. However, syrosingopine seems to offer a distinct advantage over the other preparations where such effects are to be avoided or when troublesome side-reactions limit their use as antihypertensive agents.

Summary

A clinical study made of syrosingopine therapy in 77 ambulant patients with essential hypertension demonstrated this agent to be effective in reducing hypertension, although the daily dosage required is higher than that of reserpine. Severe side-effects are infrequent, and this attribute of syrosingopine is its chief advantage over other Rauwolfia preparations. The drug appears useful in the management of patients with essential hypertension.

Addendum

Since this paper was submitted, we have observed a striking result of syrosingopine in a 45-year-old hypertensive man with recurrent angina at night precipitated by disturbing nightmares. Substitution of syrosingopine, 1.0 mg. per day, for the previously administered reserpine, 0.5 mg. per day, abolished the dreams and the angina. The blood pressure remained at its reduced level.

The syrosingopine used in this study was supplied as Singoserp (Su-3118) by Ciba Pharmaceutical Products Inc., Summit, N. J.

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APPLICATION OF ABDOMINAL PRESSURE FOR ARTIFICIAL RESPIRATION

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A method of providing long-term respiratory assistance by intermittent abdominal pressure was tested in 15 patients with respiratory paralysis of different degrees of severity. Effective artificial respiration was provided by means of rhythmic inflation of a rubber bladder incorporated in an abdominal corset. A positive displacement pump powered by line current or 24-volt battery connects to the respirator by means of a flexible plastic base. Active assisted expiration is followed by passive inspiration due to gravitational pull on the diaphragm. Ventilation improves progressively as the trunk is flexed from 30 degrees to an optimal angle of 75 degrees above the horizontal. It was not necessary to exceed pressure of 50 cm. of H_2O at 16 cycles per minute in any patient. This method increased the range of physical activities and improved vocational potentialities for those needing life-long respiratory assistance after they have had poliomyelitis.

The rehabilitation program and daily activities of patients with residual respiratory paralysis after having poliomyelitis are often limited by the types of respiratory aids now generally available. This is true despite the fact that virtually every patient, no matter how severely affected, is now emancipated from the tank respirator at least for several hours daily. The introduction of the cuirass type of respirator has greatly increased the mobility of the patient with respiratory paralysis. The rocking bed has made it possible for many patients to sleep in comfort and to enjoy relative freedom from mechanical devices during the day. Positive pressure respirators applied by mouthpiece or trachea tube have also afforded many advantages, particularly during exercise programs and to facilitate nursing care.

Each of these devices, however, has its distinct disadvantages and interferes in one way or the other with activity. The rocking bed is only slightly less restricting than the tank, since it confines the patient to one place and limits his activity while the bed is in motion. The chest-abdomen and chest cuirass respirators are bulky and conspicuous, permit little trunk motion, and interfere with the use of upper extremities in work on tables or wheel chair trays. Intermittent positive pressure respirators require the use of cumbersome hoses, and, if mouthpieces are used, they interfere with conversation, mouth wand activities, and eating. (The mouth wand is used for activities such as page turning, typing, operation of microswitches and special telephones, and painting with oils.) The need for some type of respiratory assistive apparatus which would permit maximum breathing for activities, including work at a desk, led to the perfection of the new device to be described here.

Intermittent Abdominal Pressure Respirator

The intermittent abdominal pressure respirator (Pneumobelt), hereafter referred to as IAPR, differs in principle from the conventional devices used in the United States. It produces artificial respiration by assisting expiration rather than inspiration. It consists of an elastic inflatable flat bladder incorporated within an abdominal corset (fig. 1). As the bladder inflates the abdominal wall is compressed, the diaphragm rises, and expiration occurs; when the bladder deflates the abdominal contents and diaphragm fall as a result of gravitational pull and inspiration occurs passively. Three different corset sizes (12 in., 10 in., or 8 in. long), together with adjustable straps and movable buckles, enable satisfactory fitting to various abdominal girths and lengths. The bladder may be easily removed from or inserted into the belt. The corset is constructed of washable, preshrunk cloth and with minor adjustments of the clothing may be worn under ordinary street attire.

Cyclic inflation of the IAPR is provided by a specially constructed respirator pump (Multilung), with use of a flexible, lightweight, plastic hose connection. The respirator consists of a double-acting positive displacement piston unit driven by a 24-volt, DC-geared motor. The pump is designed to provide three types of respiratory assistance: (1) intermittent positive pressure to the airway, (2) intermittent negative pressure with cuirass respirator (the pump is of sufficient capacity to provide ventilation in patients using all sizes of chest respirators and sizes A and B [Technicon-Huxley] chest-abdomen cuirass respirators), and (3) intermittent positive pressure to the abdominal wall (fig. 2 and 3). It can also deliver intermittent positive pressure (via tracheostomy, naso-oral mask, or mouthpiece)

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simultaneously with negative pressure (chest cuirass respirator), or it can provide positive pressure (via tracheostomy, naso-oral mask, or mouthpiece) synchronously but in inverse phase with positive pressure to the abdomen via the IAPR. The inspiratory phase of the IAPR is arbitrarily fixed at 40% of the respiratory cycle and the expiratory phase at 60%.

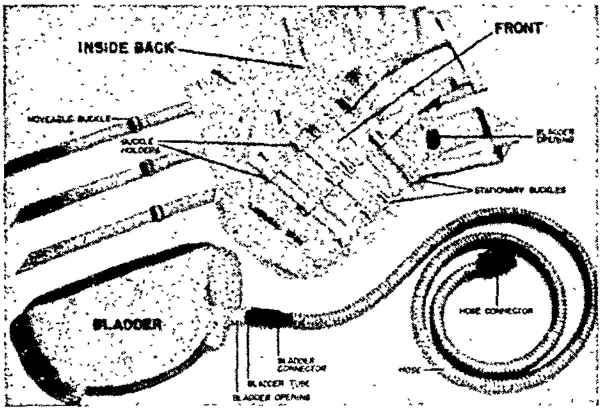

Fig. 1.—Intermittent abdominal pressure respirator: inflatable bladder and abdominal corset.

A 24-volt storage battery in a case complete with charger, charger timer, and safety fuses is provided with the unit. This battery will operate the pump for about eight hours when fully charged. The power unit contains its own rectifier so that it may be operated on 110-volt AC from a standard home utility outlet without additional accessories. Its size allows convenient placement between the rear wheels of a wheel chair. The power unit and battery charger are mounted on a small aluminum caster carrier which permits easy portability of the two parts as a unit (fig. 4). Special features of the power unit include an alarm system for power failure, respiratory rate control, independent pressure controls, a pressure safety valve, and a special intake tube to allow humidification or administration of aerosols or noninflammable gas mixtures through the positive pressure outlet for mask or tracheostomy. When the line electric current is discontinued there is automatic switchover to battery and automatic switchback to line current on its resumption. The pump can be operated manually with a hand crank on failure of line and battery current.

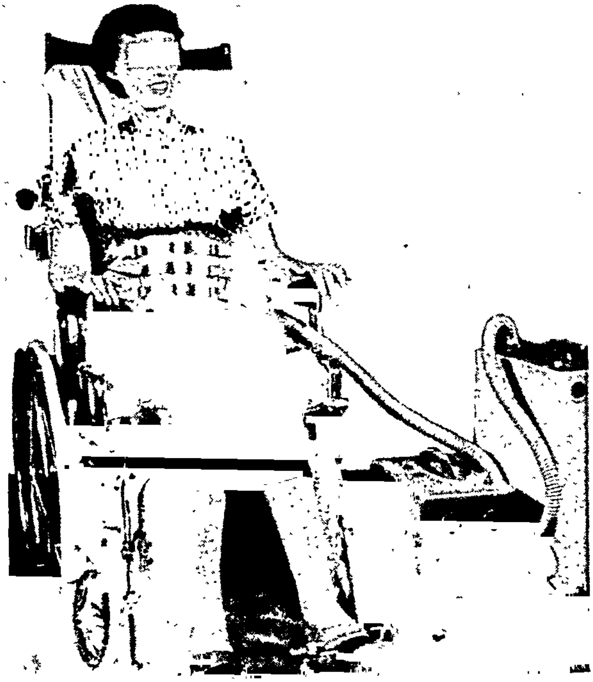

Fig. 2.—Intermittent abdominal pressure respirator with respirator pump, providing intermittent positive pressure to abdominal wall.

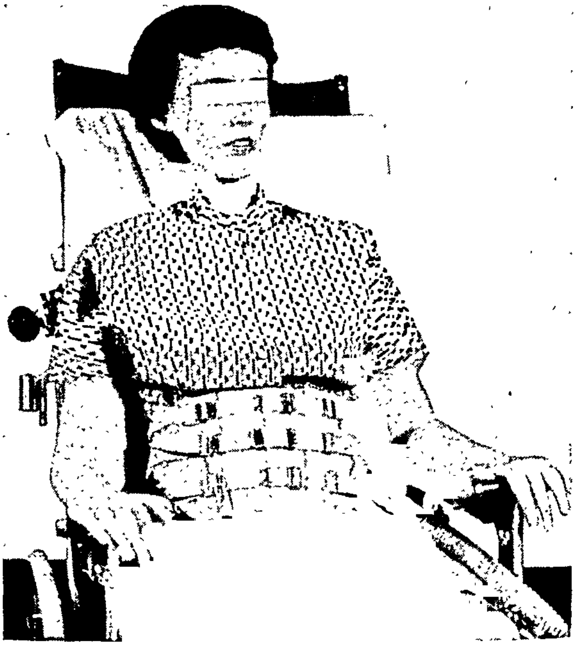

Fig. 3.—Intermittent positive pressure supplied to abdominal wall.

Testing the Respirator

Evaluation of the effectiveness of the IAPR as a method of artificial respiration was made on 15 adult subjects with paralysis of respiratory musculature due to poliomyelitis (see table).

All subjects used mechanical respiratory aids for variable periods during the day. Only three subjects had vital capacities of over 1,000 ml. Preliminary observations were also made on the use of the IAPR in the treatment of patients with pulmonary emphysema.

Subjects in a semireclining position on a stationary rocking bed were fitted with the IAPR if necessary while using positive pressure from the pump. The IAPR was then cyclically activated and the pressure gradually raised until the patient stated tidal exchange was sufficient and he was able to discard the mouth positive unit. Ventilation measurements, with use of the 9-liter Collins spirometer, were made with the patient's trunk inclined to several angles with respect to the horizontal plane and at several pressure settings for each angle. All subjects were instructed to relax as much as possible in order to permit the IAPR to take over the work of breathing. Whenever possible, arbitrary IAPR pressures of 20, 30, 40, 50, and 60 cm. H_2O and trunk angles of 30, 40, 60, and 75 degrees were selected for ventilation measurements. Eight to 10 respiratory cycles were measured, and averages were determined for each pressure and angle. Measurements were discarded as unreliable if there was more than 10% variation of tidal volume in these 8-10 cycles.

Effectiveness of Intermittent Abdominal Pressure Respirator in Fifteen Patients

Case No.	Sex	Age, Yr.	Time Since Onset, Mo.	Height, In.	Weight, Lb.	Vital Capacity, Ml.	Required* Daytime Tidal Volume, Ml.	Minimum Required† IAPR Pressure, Cm. H_2O
1	M	19	12	71	100	50	320	18
2	F	27	15	68	100	300	315	30
3	M	39	43	65	145	325	430	49
4	F	23	36	66	130	375	310	50
5	F	32	6	66	90	400	290	39‡
6	M	26	13	72	153	410	450	27
7	F	30	3	65	94	450	290	27
8	M	32	6	71	103	500	365	19‡
9	F	21	60	61	100	600	310	42
10	M	18	13	71	140	610	420	28
11	M	26	13	72	140	700	430	17
12	F	25	25	68	168	800	420	38
13	M	34	5	73	125	1,100	410	18
14	M	35	36	73	130	1,250	400	28
15	M	27	10	65	129	1,450	400	27

* At 16 breaths per minute.
† To achieve tidal volume in 75-degree sitting position.
‡ 60-degree sitting position.

As previously mentioned, the IAPR is incorporated in three different corset sizes to enable fitting different body builds. This study did not specifically investigate ventilation differences produced by the different corset sizes in individual subjects. Choice of corset size used is based largely on the subject's build and his comfort. In general, the large size fits adult males; the medium, adult females; and the small, children. Two points regarding application of the corset deserve consideration: If the corset is applied too snugly or too loosely the IAPR loses effectiveness. Trial and error application is necessary to find the precise tightness which produces both optimal ventilation and comfort for the subject. The corset is designed with a convex lower border (to fit the suprapubic area) and a horizontal upper border. It should be applied with its upper border approximately at the level of the xiphoid in order to insure enclosure of the lower portion of the rib cage. Preliminary studies in some subjects revealed a tendency to paradoxical expansion of the chest with application of abdominal pressure. This tendency was found to be minimized by enclosure of the lower thorax by the corset.

Results of Testing

Relation of Tidal Volume to IAPR Pressure.—Figure 5 shows data obtained from three subjects in a 75-degree sitting position at various IAPR pressures. Good correlation is obtained between the pressures applied at the belt bladder and the tidal volumes measured. All other subjects showed a similar roughly linear correlation between the IAPR pressure and tidal exchange. It was noted, however, that there was marked variation from subject to subject in the absolute tidal volumes obtained at the same IAPR pressures as well as in the slope of the lines relating tidal volume to pressure. The range of variation in the "compliance" values derived from the tidal volume pressure grafts was from 3 ml. of tidal volume per cubic centimeter of water rise in IAPR pressure to approximately 90 ml. per cubic centimeter of water pressure. The reasons for the wide variation in compliance from patient to patient are probably numerous. Incomplete relaxation of subjects with unconscious resistance or assistance to air flow may be an important factor. It is recognized that valid measurements of tidal exchange could probably be made only with the patient completely under curarization. This was not feasible in this study. However, in order to minimize errors due to variation in the degree of relaxation of each subject, measurements were considered reliable only if there were little variation in the 8 to 10 tidal volumes recorded for each IAPR pressure and bed angle. Other factors concerned, in addition to pulmonary and thoracic cage compliance, may be variation in effective abdominal length and compliance of the diaphragm, abdominal wall, and related structures.[1]

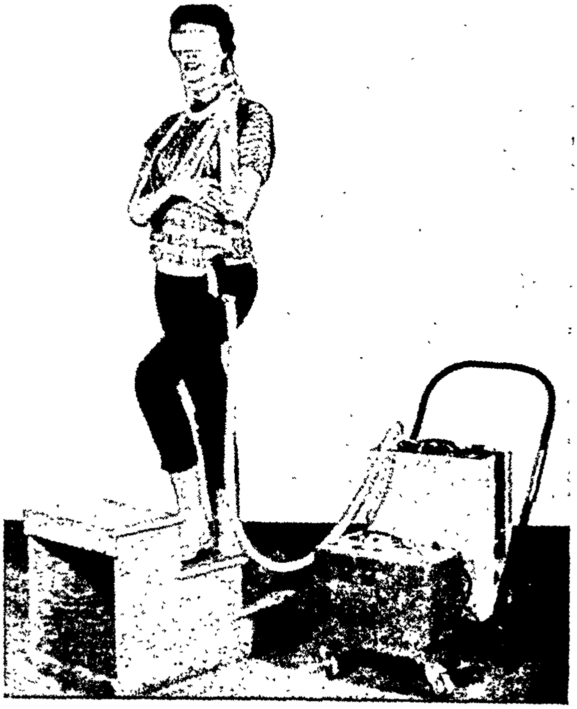

Fig. 4.—Easy portability of respirator unit.

Pressures of 50 cm. H_2O and below were uniformly comfortably tolerated. Pressures above 70 cm. H_2O usually made the patient uncomfortable. No subject was encountered who did not achieve an adequate tidal exchange at a pressure of 50 cm.

H_2O in the 75-degree sitting position. All subjects could, of course, undergo hyperventilation if pressures higher than those necessary to achieve adequate tidal volumes were used. The table shows the minimum IAPR pressure required for each subject to achieve an adequate tidal volume in the 75-degree sitting position. (Required tidal volumes were estimated from the Radford nomogram at a respiratory rate of 16 per minute.[2])

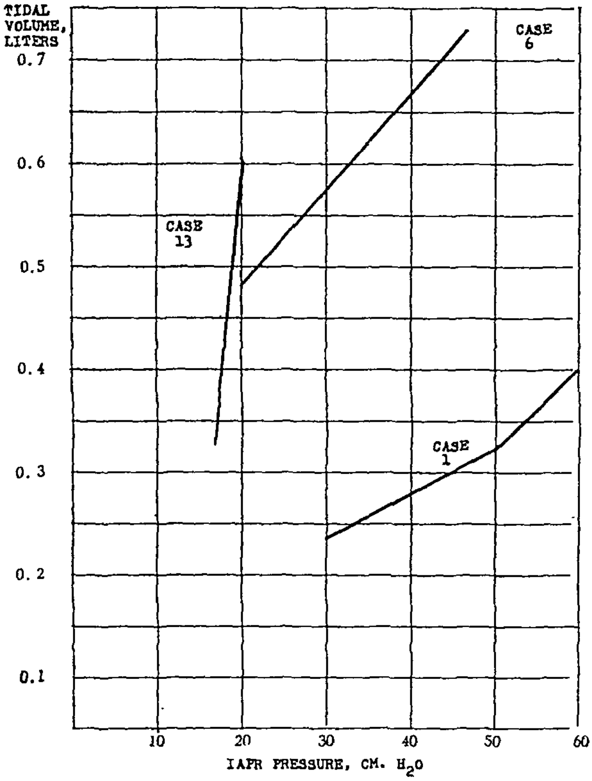

Fig. 5.—Tidal volume and required pressures in three subjects using intermittent abdominal pressure respirator.

Relation Between Tidal Volume and Angle of Trunk with Respect to Horizontal Plane.—Figure 6 shows the data obtained from a 25-year-old quadriplegic woman (case 12, see table) with a vital capacity of 800 ml. Tidal volume is shown at four different angles of the trunk with respect to the horizontal plane. It can be seen that tidal exchange is progressively improved as the subject moves from the semireclining to the sitting position. All subjects showed a roughly similar increase in tidal volume with progressive increase in body inclination from the horizontal to the vertical position. In general, the IAPR proved inadequate to move sufficient air with the subject supine. Under the conditions of measurement, inspiration is passive and dependent on the action of gravity on the abdominal contents and diaphragm. Therefore, the IAPR would not be expected to function with the subject recumbent. While one subject has been able to use the IAPR for comfortable sleeping at a reclining angle of 15 degrees, in most subjects 25 to 30 degrees is the minimal angle at which adequate ventilation can be achieved.

Comment

Use of IAPR in Rehabilitation Program.—In the rehabilitation of the patient with respiratory paralysis during the past decade emphasis has changed from a goal of freedom from respiratory aid to one of safe, maximum function.[3] This has been made possible by provision of the patient with severe paralysis with the precise amount of respiratory assistance necessary for the various activities of daily living. The IAPR has been found to be a valuable adjunct to the cuirass and positive pressure respirators in permitting this type of patient to pursue an active exercise program without developing hypoxia. We consider this device to be the respirator of choice for such activities as stair-climbing (fig. 4) and those exercises, especially of the upper extremities, best performed with the subject in the sitting position. It is also the most acceptable respiratory aid for patients who can use it for vocational activities in the sitting or standing positions.

Some patients with pronounced trunk weakness require specially designed, tailor-made body corsets in which the IAPR bladder may be simply incorporated. It may be of interest that, on at least one occasion (in work done by Dr. B. C. Kriete at the Respiratory Center of Goldwater Memorial Hospital, Welfare Island, N. Y.), the IAPR bladder has been placed under the plaster-of-Paris body jacket of a patient with scoliosis and the patient was successfully given ventilation while the cast had to be worn.

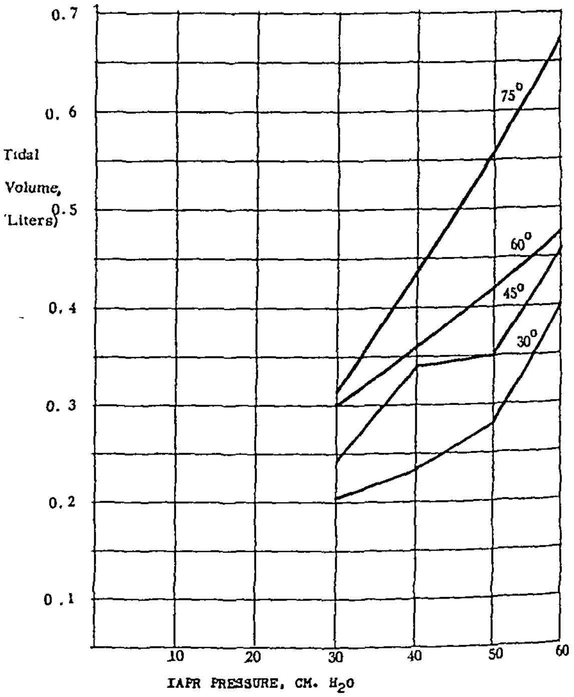

Fig. 6 (case 12).—Tidal volume and required pressures at four angles of trunk.

Use of IAPR in Nonparalytic Pulmonary Diseases.—At the present time the IAPR is used principally for long-term respiratory assistance of patients with respiratory paralysis due to poliomyelitis. Although it has been recognized that increased work of breathing plays an important part in the pathogenesis of respiratory acidosis due to chronic pulmonary disease, few workers have used prolonged respiratory assistance with mechanical respirators to relieve the work of breathing.[4] Preliminary observations on the use of the IAPR in three patients with respiratory acidosis due to chronic pulmonary emphysema have impressed us with the value of this device for such a purpose. Since pulmonary emphysema is associated with increased functional residual capacity and expiratory difficulty, it would seem that correction of the pathomechanics would be aided more by use of IAPR than by the more commonly employed positive pressure breathing devices. Further work is in progress to document these impressions and to delineate the place of this respirator in the over-all management of patients with this disease.

Summary and Conclusions

A new mechanical respirator, operating on the principle of assisted expiration through intermittent abdominal pressure, has proved effective as a ventilatory aid in a group of 15 patients with respiratory paralysis. Adequate ventilation of all subjects was accomplished with less than 50 cm. H_2O applied to the abdomen with the subjects in a sitting position. Ventilation rose progessively as the subjects' trunks were raised from the recumbent to the sitting position and, similarly, as the abdominal pressure was increased. The respirator has been found to be a valuable adjunct to other respiratory aids in permitting rehabilitation activities without hypoxia. For some activities it is the respirator of choice. Preliminary observations in patients with pulmonary emphysema suggest that this new respirator may have a definite place in the over-all management of this disease.

Fairmont Hospital of Alameda County, Foothill Boulevard (Dr. Lewis).

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The test equipment used in this study was supplied by Conitech, Ltd., Chauncey, N. Y.

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COLD ADAPTATION.—The natives who volunteered for the tests were all young males of the Pitjandjara tribe of the arid, semi-desert country of central Australia. Around the native settlement at Areyonga they wore clothing, usually shirt and trousers and, sometimes, boots. They informed us through the superintendent, who spoke their language, that usually they removed their clothing at night, using it as a pillow, and invariably they did this while out hunting. . . . We were here interested in analyzing the response of natives and ourselves sleeping "proper bush", i.e. nude between fires in the native way. The natives were therefore asked to arrange the windbreak and fires for the night according to their accustomed manner. The men then stripped and lay down either singly or back to back between the fires. They took care of stoking the fires themselves and this occurred some 3-10 times during the night. They lay motionless between stokings and apparently slept well, frequently snoring. . . . The metabolic and thermal response was investigated by measuring oxygen consumption and rectal, skin and environmental temperatures throughout the night. . . . The great heating of the skin towards the fire and the considerable cooling towards the shadow, i.e. the sky or another man, are very striking. Skin temperatures were regularly found to be lower in the natives than in the whites. . . . Natives sleeping 'proper bush' and stoking the fires at their own volition often had skin temperatures in the shadows as low as 12-15°C and, facing the fire, sometimes exceeding 45°C. . . . Such temperatures, which must be regarded as of normal occurrence in the natives, are painful to white men. In contrast, measurements in our own regular sleeping gear showed that all our skin temperatures, including that of the foot, remained above 33°C throughout the night. With a much greater latitude of tolerance to chilling and relatively few interruptions for fire tending, the native can rest and sleep through cold nights.—P. F. Scholander, H. T. Hammel, J. S. Hart, D. H. LeMessurier, and J. Steen, Cold Adaptation in Australian Aborigines, *Journal of Applied Physiology*, September, 1958.

CLINICAL NOTES

SHORT DISTANCE RADIO TELEMETERING OF PHYSIOLOGICAL INFORMATION

F. Lowell Dunn, M.D.
and
Harold G. Beenken, E.E., Omaha

Current development of transistors and electronic circuitry provides an opportunity for further advances in the development of portable equipment for studying physiological function in ambulant and working subjects.[1] With encouragement, about four years ago we began the design of a portable transmitting and recording system. Objectives were as follows: the transmitter should be compact and not over 2 lb. in weight; the system should transmit the frequencies encountered in most physiological studies, i. e., 0 to 1,000 cps; the system should transmit and record more than one channel simultaneously; the transmitter should transmit all channels requiring only the addition of suitable transducers and preamplifiers for the various types of physiological information desired; and the system should be operable by persons without radio engineering experience. Electrocardiographic transmission was selected for the first design because it represents an important band of physiological frequencies and we were familiar with the circuit problems. We wish to describe here the present model. Electronic details will be described elsewhere.[2]

After a number of preliminary assemblies a system was constructed transmitting at 540 kilocycles per second. The weight was over 2 lb. because of the necessity of using vacuum tubes in several stages requiring filament and high-voltage batteries. A study of Federal Communications Commission (FCC) data showed that the 540-kilocycle region had a high noise level in such buildings as hospitals and that this noise level was too high for reliable operation under the FCC low-power radiation rule. In 1954 it was not obvious how rapidly transistors would improve, but by 1956 noise levels were down, greater uniformity in production was being achieved, and operation was successful in megacycle ranges. The advantages of operation in the megacycle range are great. At 100,000,000 cps, equipment components would be smaller and battery consumption much less, there would be the advantage of using frequency modulation for transmission, and the design of a multichannel assembly would be simplified.

Transmitting System

Figure 1 shows a block diagram of the transmitting system. The patient is connected to the electrocardiogram preamplifier by means of three electrodes properly placed to get the desired recording. The electrode signals 2 to 3 mv. maximum with an average of 6,000 ohms source impedance and is amplified by the electrocardiogram preamplifier to such a level that the 3-mv. signal results in 90 to 95% amplitude modulation of audio frequency. The audio oscillator is tuned to the carrier frequency of the channel involved. In this unit it is 2,100 cps. Design considerations are for multichannel operation, up to a maximum of 10 channels. The carrier frequencies of the first six channels are 600, 1,350, 2,100, 2,850, 3,600, and 4,350 cps. These channels will have a band width of 170 cps at the 1-db. points, 250 cps at the 3-db. points, and 275 cps at the 6-db. points. The next four channels will have nominal band widths of 1,000 cps each. The exact carrier frequencies of these four channels have not been determined but will be between 6,000 and 15,000 cps. The amplitude modulation of the audio frequency also takes place in this block.

The amplitude modulation (AM) signal is then amplified in the next block to proper power level to frequency modulate the following stage. AM signals from other channels will be combined in this stage.

The last block in the transmitting system includes the radio frequency oscillator oscillating at 104 megacycles per second and the circuitry for fre-

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quency modulation (FM) of this frequency with the combined AM signals from the channels.

The system of AM-FM is being used. FM of the radio frequency was chosen because of its inherent advantages over AM in signal to noise ratio and because the field of transistors has developed enough to allow operation at the very high frequencies where FM is desirable. Double side band AM of the audio channel frequency is used because a simple detector can be used without supplying a demodulating frequency that has to be kept at the same frequency as the channel frequency. Small drifts of the channel frequency do no harm as long as the frequency is satisfactorily inside the pass band of the receive band pass filter.

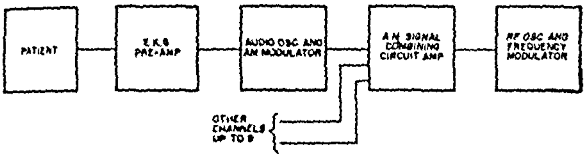
PATIENT
E.K.G. PRE-AMP
AUDIO OSC AND AM MODULATOR
A.M. SIGNAL COMBINING CIRCUIT AMP
RF OSC AND FREQUENCY MODULATOR
OTHER CHANNELS UP TO 8

Fig. 1.—Block diagram of transmitting system.

A block diagram of the receiving system is shown in figure 2. The receiving antenna is a four-element beam with a driven element, reflector, and two directors. The FM receiver can be any good receiver covering the frequency band involved.

The output of the receiver is impedance matched by means of an L pad, if required, to the 600 ohm input of the band pass filters. The channels are separated by means of these receive band pass filters. One receive band pass filter is used for one-channel operation, two for two-channel operation, etc. The output of the receive band pass filter is connected to a conventional diode detector. The output of the detector is connected to a low pass filter. This low pass filter passes the desired detected intelligence from direct current to 300 cps and attenuates audio carrier frequencies and harmonics due to detection by more than 50 db. The output of the low pass filter is terminated in its characteristic impedance of 10,000 ohms and can be connected to almost any recorder of greater than 10,000 ohms input resistance and greater sensitivity than 1 volt full scale. Other recorders could possibly be used with proper circuit matching pads. In electrocardiogram transmission, enough loss is inserted in the receive circuit so that a conventional electrocardiogram recorder can be used.

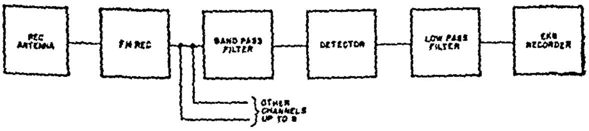

Fig. 2.—Block diagram of receiving system.

Miniaturization of the transmitting system has been accomplished to the extent that no large circuit components are required. The power supply requirements are very low because the transmitter is completely transistorized. Our test model used mostly standard-size circuit components as a convenience in making changes dictated by test results. Use of miniature and subminiature components and assemblies would greatly reduce the size of the system. Figure 3 shows the single-channel electrocardiogram model. Battery current for the preamplifier and audio oscillator is approximately 2 ma. and for the radio frequency circuit 3 ma. Battery life is approximately 100 hours. An antenna was not used. To be nondirectional, an antenna would have to extend several feet above the head. Aside from being conspicuous it would interfere with walking through doorways. Radiation is obtained direct from the tuned oscillator circuit, i. e., two turns 1¼-in. diameter of no. 14 tinned wire, which can be seen in figure 3. This provides a transmitter which is essentially nondirectional,

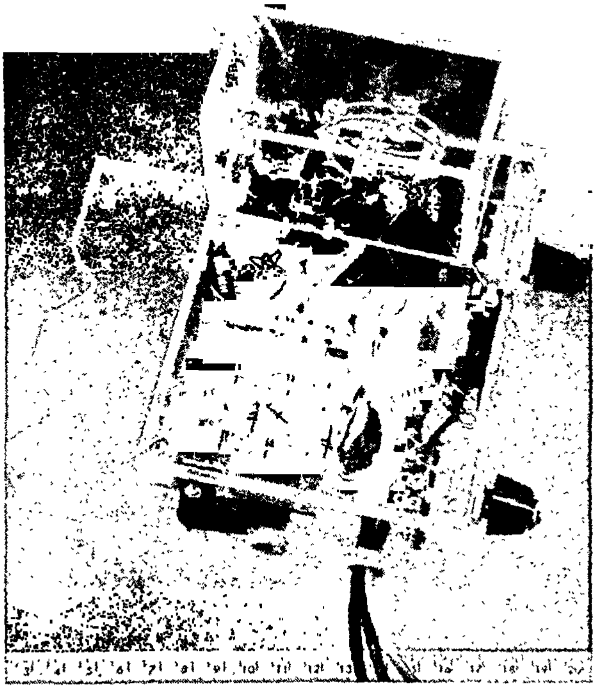

Fig. 3.—Complete transmitter with single channel for electrocardiogram transmission, with band width of 250 cycles and time constant of 4 seconds operating at AM carrier frequency of 2,100 cps and FM frequency of 104 megacycles per second.

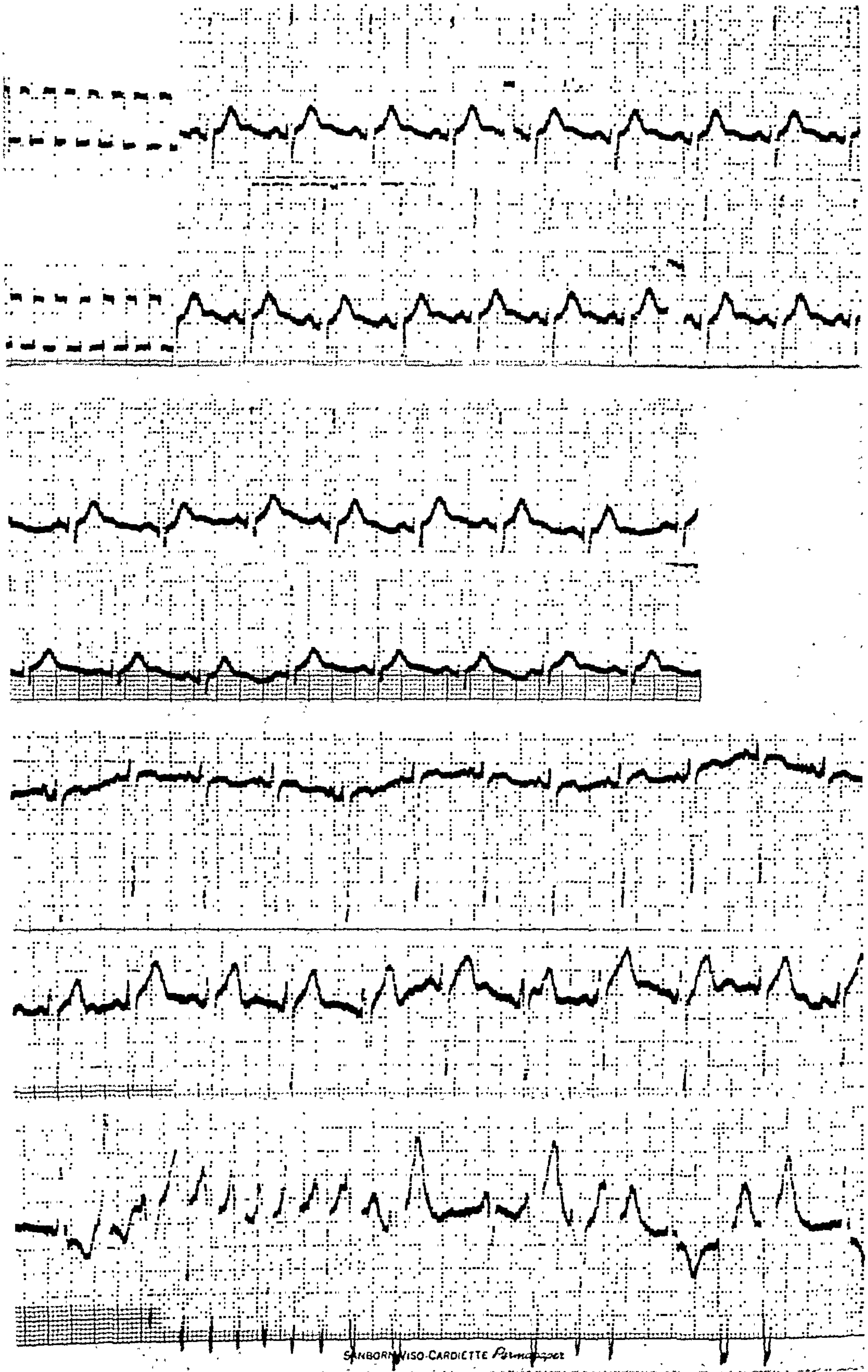

Fig. 4.—*Top tracing*, standardization, 1 mv., and electrocardiogram from direct-writing electrocardiograph. *Second tracing*, standardization and electrocardiogram from same subject with use of radio transmitter and recorded by same electrocardiograph. *Third tracing*, transmitter 100 ft. from receiver, fastened to subject's back, which was toward receiver. *Fourth tracing*, subject facing receiver. *Fifth tracing*, subject walking in corridor. *Sixth tracing*, subject walking on treadmill. *Seventh tracing*, short run of ventricular tachycardia while subject was walking on treadmill.

and calibration is maintained over the working distance. Operating distance is about 200 ft. indoors and over 500 ft. outdoors. Larger transistors, which should be available to us soon, will increase the working distance to a half mile, which appears to be a maximum for projects presently contemplated. The transmitter is stable in operation, does not require any field adjustments, and is not affected by shaking. During construction the transmitter was tested and adjusted for uniformity of operation over the range of 70 to 90 F. The electrocardiogram preamplifier works satisfactorily over the range of 60 to 106 F.

The one-channel model reported here was used for electrocardiogram transmission. This meant that the preamplifier had to amplify signals of 0.1 to 3 mv. in the presence of skin potentials of a possible amplitude of 50 to 100 mv., have a time constant of 4 seconds, have at least 200,000 ohms input impedance, maintain a steady base line, and have adequate rejection of inphase signals.[3]

Clinical Use

Figure 4 shows samples of records. A calibrating signal of 1 mv. is provided in the preamplifier. Transmission of records is without loss of fidelity, and the time constant of 4 seconds is sufficient to transmit the slower changes in the electrocardiogram without loss of amplitude.[3] Tracings 3 and 4, taken with the subject standing 100 ft. from the receiver, show that position does not affect fidelity of the transmission. Tracings 5 and 6 were taken with the subjects walking in the hall and on a treadmill. The front electrode is in V_3 position, and the back electrode is at the same level and ½ in. to the right of the midline. Tracing 7 shows the sudden onset of a ventricular tachycardia in a young man. The immediate recording permitted diagnosis and cessation of the exercise promptly before his severe type of attack developed.

By the use of available transducers and the construction of proper preamplifiers, the transmitting system can be applied to counting, temperature, pressure curves, curves requiring base-line stability and calibration, and electrical and mechanical sensing. A few of the applications that have been discussed are as follows: electrocardiograph monitoring of exercise tests; combination of two electrocardiograms to produce a vector that will give maximum sensitivity to T-wave changes as an index of anoxia during exercise testing; electrocardiogram monitoring during conferences where strain patterns are introduced; rectal temperature and/or electrocardiogram in a tractor operator working in a field; electroencephalographic monitoring in ward or conference; electromyographic or myographic multichannel recording for diagnosis or for study of phases of coordination in retraining; pressure measurements from various locations of the foot and shoe during walking; and monitoring electrocardiograms in operating or recovery room without connecting wires.

Several other features should be mentioned. Modern medical practice often utilizes formidable masses of instrumentation both in the ward and in the operating room. The stability and ease of operation of this transmitter offers the possibility of eliminating a few of the wires draped around the subject and at the same time notably reduces possible explosion hazards due to the very low voltages used and the completeness of shielding possible. This isolation of the transmitter makes it much less susceptible to stray fields, artifacts, and noise.

Summary

A completely transistorized radio transmitter and receiving system operates at 104 megacycles per second. The weight is under 2 lb., without the use of miniature parts. Design is for transmission of up to 10 channels with band widths of 150 to 1,000 cps. The channel reported has a carrier frequency of 2,100 cps and was tested for electrocardiographic recording. Satisfactory calibrated records were obtained with subjects walking and on the treadmill.

University of Nebraska College of Medicine, 42nd and Dewey Avenue (5) (Dr. Dunn).

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Ronald D. Loch supplied technical assistance in this study.

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CORTICOSTEROID TREATMENT OF TRANSFUSION REACTION FROM INCOMPATIBLE BLOOD OF ABO TYPE

REPORT OF A CASE

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Blood transfusions have become commonplace in the practice of medicine; mortality from them is approximately the same as mortality from appendectomies. Some reactions do occur, however, for various reasons, and their treatment requires prompt recognition of the type of reaction and immediate therapy. Transfusion reactions are of four types: pyrogenic, manifested by fever, chilly sensations, nausea, vomiting, and headache; allergic, manifested by urticaria and sometimes wheezing; reaction to the plasma of the blood, manifested by chills, fever, and muscular pains but no hemolysis; and finally the dreaded hemolytic reaction which is sometimes fatal.[1]

The hemolytic reaction is an antigen-antibody reaction due to blood group incompatibilities. It begins suddenly, soon after the transfusion is started. The patient becomes restless and complains of back pain, chills, fever, nausea, vomiting, and precordial oppression. The condition may progress rapidly into shock. Hemoglobinemia and hemoglobinuria appear almost immediately. Impairment of renal function usually ensues, and the patient most frequently dies from this cause. A fatal bleeding tendency may also develop.

The treatment of the patient with hemolytic reaction has heretofore consisted primarily in stopping the blood transfusion and instituting supportive measures to protect the kidney and to treat the eventual lower nephron nephrosis. Antibiotics are indicated to combat infection which may increase the breakdown of protein, and electrolytes must be carefully balanced. In spite of the fact that there are many reports of the effectiveness of ACTH and cortisone in the treatment of acquired hemolytic anemia [2] or hemolytic disease of the fetus and newborn (erythroblastosis fetalis),[3] there have been few reports in the literature of the use of these agents in the treatment of patients with transfusion reaction. The report of a patient so treated follows.

A 57-year-old woman underwent repair of a cystocele and rectocele and excision of the cervical stump on Aug. 6, 1957. She was discharged from the hospital on Aug. 15 in good condition. Shortly after going home she began to bleed slightly. On Aug. 21 she bled profusely and was readmitted to the hospital in a state of shock. Her hemoglobin level was 8 Gm. per 100 cc. She was given a transfusion on the morning of admission, without reaction, but continued to bleed slightly. She was given another transfusion on the evening of admission and again there were no ill-effects.

On the morning of Aug. 22, at 10:20 a.m., another transfusion was begun. Almost immediately she began to complain of not feeling well. The rate of transfusion was slowed. The patient complained of nausea and aching and had a severe shaking chill. Her temperature reached 103.4 F. (29.6 C). The transfusion was stopped at 10:55 a.m. after almost 200 cc. had been given. A check on the blood showed that she had received type A blood and her blood was type O, Rh positive. Through a laboratory error, the wrong bottle of blood had been given her. Within one-half hour after the start of the transfusion her blood pressure had dropped to 70/50 mm. Hg from 110/60. She had a backache and was in critical condition. ACTH, 40 units in 1,000 cc. of 5% glucose in water, was started intravenously. She was also given 100 mg. of hydrocortisone sodium succinate (Solu-Cortef) intravenously and 50 mg. of cortisone intramuscularly. Intramuscular cortisone therapy was maintained in full dosages as well as ACTH gel.

Frequent laboratory studies were done on the patient. Urinalysis on Aug. 23, 1957, showed a faint trace of albumin and six to eight white blood cells per high-power field, but there were no red blood cells and no evidence of hemoglobinuria. Results of van den Bergh's test remained normal throughout. Repeated urinalyses and blood studies showed no evidence of hemolysis. Her urea nitrogen level rose slightly from 18 mg. per 100 cc. on Aug. 22 to 25 mg. per 100 cc. on Aug. 27. Her blood cell count rose steadily from a hemoglobin concentration of 8.8 Gm. and 2,700,000 erythrocytes per 100 cc. on Aug. 24 to 10 Gm. of hemoglobin and 3,340,000 erythrocytes on Sept. 2. By Sept. 2, her urea nitrogen level had dropped to 16 mg. per 100 cc. Her urine at times showed a few red blood cells and a few white blood cells but a Foley catheter was in place during this time and some of these may have been due to irritation. The patient had a good volume of urine throughout this time. She recovered and has remained well.

Summary

The literature contains many reports of the effectiveness of ACTH and cortisone in the treatment of hemolytic anemias of the acquired type or Rh incompatibilities. Corticosteroid therapy has been effective in the treatment of patients with hemolytic disease of the fetus and newborn (erythroblastosis fetalis); there are a number of reports of prevention of this disease in utero by administration of corticosteroids to the mother.[3b]

In a case of transfusion reaction ACTH and cortisone apparently blocked the hemolysis expected from an incompatible blood transfusion. Administration of corticosteroids in these medical emergencies should be added to the present program of treatment.

432 Badgerow Bldg. (1).

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SPONTANEOUS HEMOPNEUMOTHORAX IN A HEMOPHILIAC

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Despite the diversity of hemorrhagic complications encountered in patients with hemophilia, bleeding within the chest is uncommon. In 1943, review of the early literature by Freedman and associates [1] revealed only two cases of hemorrhagic disease complicated by hemothorax; neither patient was a hemophiliac. These authors reported a 22-year-old man with a familial history and laboratory studies characteristic of hemophilia, whose spontaneous hemothorax was treated successfully by repeated thoracenteses and "numerous small transfusions." A similar case had been reported by Pendergrass and Neuhauser [2] the year before. In 1957, Kay and Kupfer [3] reported a spontaneous hemothorax in a proved hemophiliac successfully treated by thoracenteses and infusions of antihemophilic globulin.

In 1953, in the Polish literature, Juszczynski [4] reported a stab wound of the chest successfully treated by thoracotomy in a presumed hemophiliac. The response of this patient to stored bank blood suggests that this was actually a case of Christmas disease and not classic hemophilia.

In a search of the literature, no previous case of spontaneous hemopneumothorax complicating hemophilia was found. Since the management of the mechanical problems of a pneumothorax complicated by intrapleural bleeding in a hemophiliac has not to our knowledge been discussed in the literature, it seems worthwhile to present the following case report.

Report of a Case

A 27-year-old man entered the emergency ward of the Massachusetts General Hospital, Boston, at 9 p.m. on July 25, 1957, shortly after the onset of left thorax and arm pain which developed while he was getting out of an automobile.

Physical examination on admission showed an acutely dyspneic, well-developed young man with a left pneumothorax. X-ray examination of the chest on admission showed 75% collapse of the left lung and a small amount of fluid at the base. Thoracentesis in the second anterior interspace was performed, with removal of 1,500 cc. of air under slight positive pressure. This procedure completely relieved the patient's dyspnea. Physical examination showed reexpansion of the left lung.

During the night his dyspnea returned. Physical examination again revealed a left pneumothorax with shift of the mediastinum to the right and fluid at the left base. Aspiration of 1,500 cc. of air from his chest was done, and near normal breath sounds returned and his dyspnea disappeared.

On admission a history suggestive of hemophilia had been given, and an infusion of fresh frozen plasma was begun. At this time his hemoglobin level was 15.5 Gm.%, white blood cell count 8,300 per cubic millimeter with a normal differential, bleeding time 7 minutes,[5] and clotting time 16 minutes.[6] The number of platelets appeared normal on the smear. Stool guaiac examination and urinalysis gave negative results.

By morning he again began to feel short of breath, and x-ray examination showed a total collapse of the left lung with fluid present to the level of the sixth interspace posteriorly and a shift of the mediastinum to the right. Because of the continued signs of tension, a catheter was placed through the eighth interspace in the posterior axillary line under 10 cm. of water negative pressure. Aspiration of 1,000 cc. of blood was done. There was a moderate pulmonary air leak, as judged by the steady aspiration of air from the chest. Laboratory studies showed a hemoglobin level of 15.0 Gm.%, platelet count of 343,000 per cubic millimeter,[7] normal clot retraction with no lysis, prothrombin time 100%,[8] and prothrombin consumption 84%.[10] However, at

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the time these tests were done he had received 300 cc. of fresh frozen plasma and 500 cc. of fresh blood.

The patient had bled easily after minor trauma since childhood. A tonsillectomy at the age of 7 years was followed by profuse hemorrhage requiring packing and transfusion. A subsequent tooth extraction and a cheek laceration had each required transfusion. He had been studied in 1937 at the Boston City Hospital, where a diagnosis of hemophilia had been made. His maternal grandfather was a "bleeder" and had died of hemorrhage. His brother had also bled severely after minor lacerations. There was no history of abnormal bleeding in his mother or other members of the immediate family.

Despite catheter drainage the lung remained completely collapsed. A second catheter was placed in the second anterior interspace in the midclavicular line the evening of the first day. During the first 24 hours 3,000 cc. of blood was drained from his chest tube and there was evidence of a continued pulmonary air leak. During this period he had been on a regimen of 100 cc. of fresh frozen plasma per hour, quantitative replacement of blood loss by fresh blood transfusions, and administration of Vitamin K, ascorbic acid, and antibiotics. Although his clotting time was normal, he continued to bleed. In the second 24 hours 2,500 cc. of blood was drained from his chest despite replacement with fresh blood and fresh frozen plasma. Treatment with 120 mg. of prednisone in four divided doses was begun. X-ray examination showed the mediastinum to be shifted to the right and his lung totally collapsed despite the two catheters.

On the third hospital day the bleeding, as measured by the chest catheter drainage, slowed and by the fourth day had stopped. The fresh frozen plasma infusion was reduced to 100 cc. every three hours, and the upper tube was removed. On the sixth day he was comfortable. Clotting time was three and one-half minutes. The remaining catheter was removed. The amount of fresh frozen plasma given was reduced to 500 ml. per day.

On the ninth day purulent drainage from the lower catheter wound appeared, his temperature rose to 103 F (39.4 C), and it was apparent that he had an empyema. Culture showed Staphylococcus pyogenes var. aureus sensitive to chloramphenicol (Chloromycetin) and erythromycin. Treatment with this combination of antibiotics controlled the systemic infection, and the empyema drained spontaneously through the previous stab wound in the lower left chest. He was discharged on Aug. 27, 1957, with a chronic draining empyema.

He was readmitted on Sept. 7, 1957, because of persistence of fever, weight loss, and malaise. A catheter was inserted into the left chest, but adequate drainage could not be established. Rib resection, which had been previously rejected because of the danger of bleeding, was now elected. In order to be sure that bleeding could be controlled, a test incision was made through the superficial tissue down to the eighth rib in the postaxillary line after 800 cc. of fresh frozen plasma had been given. This was closed, and postoperative bleeding was not a problem. On the following day a 4-cm. segment of the eighth rib was excised by reopening the test incision after a second priming dose of 800 cc. of fresh frozen plasma. Free open drainage of the left thorax was established. Over the next two weeks his temperature declined, although his general status was unimproved, and he was sent home on Oct. 18, 1957, for convalescence.

In the succeeding six weeks he continued to lose weight and to run a low-grade fever at home; he was admitted on Nov. 29, 1957, for reevaluation. On admission there was marked muscle atrophy of the left chest. He appeared chronically ill and wasted. There was a bronchopleurocutaneous fistula. Culture of the empyema drainage showed Staph. pyogenes var. aureus and Bacillus pyocyaneus. The left lung was collapsed, and there was marked thickening of the parietal and visceral pleura by x-ray. Laboratory studies showed the following findings: hemoglobin level 11 Gm.%, white blood cell count 13,000 per cubic millimeter, platelets 627,000 per cubic millimeter, clotting time 20 minutes, one-stage prothrombin time 100%, prothrombin consumption 75%, thromboplastin generation 25%,[11] antihemophilic globulin level 40%,[12] Christmas factor level 80%, factor V level 120%,[14] factor VII level 50%,[15] and fibrinogen level 400 mg. %.[16] His clotting defect was readily corrected in vitro by the addition of fresh normal plasma but not by the addition of plasma from a patient with classic hemophilia.

Because of his progressive downhill course and bronchopleurocutaneous fistula, it was felt that early death was inevitable unless the septic process could be controlled. Conservative measures, which had been previously elected because of his bleeding defect, had failed and it appeared that only decortication, reexpansion of the lung, and closure of the fistula would reverse the decline.

Since coagulation studies showed him to have a relatively mild degree of hemophilia and the surgically induced bleeding during the rib resection for drainage of his empyema had been easily controlled, it was felt probable that his bleeding disorder could be managed with fresh frozen plasma.

In preparation for operation he was given 800 cc. of fresh frozen plasma during the induction of anesthesia. This raised his thromboplastin generation, antihemophilic globulin level, and Christmas factor level each to 100% of normal. A visceral and parietal decortication with good expansion of the lung was carried out through a left lateral thoracotomy in the fifth interspace. The bronchopleural fistula was found in the posterior segment of the upper lobe, where dense adhesions held the atelectatic segment to the chest wall. This was easily closed. Bleeding was meticulously controlled with fine ligatures where possible and with the electrocautery on surfaces where ligatures could not be used. Bleeding during the procedure was not excessive, and all losses were immediately replaced with fresh whole blood.

He received 2,000 cc. of fresh blood the day of operation. In the first two postoperative days his chest tubes drained 1,800 cc. of blood, which was replaced with transfusions of fresh blood. In addition, he received 100 cc. of fresh frozen plasma per hour. By the third day his hemoglobin level was 9 Gm.%. He received an additional 1,200 cc. of fresh blood. It appeared that he was accumulating a large, clotted, left hemothorax. The mediastinum shifted to the right and the chest catheters ceased to drain. He became dyspneic, and by the fifth postoperative day his respiratory status had become so precarious that the incision in the left side of the chest was reopened with the patient under cyclopropane anesthesia and 2,300 cc. of clotted blood was evacuated. No specific bleeding point could be identified. While the chest was being closed, heart action suddenly ceased. Manual systole was immediately instituted with resumption of normal sinus rhythm after a minute of massage. The incision was then closed, whereupon he developed ventricular fibrillation. Electrical defibrillation was performed, but manual systole for 1 hour and 48 minutes failed to restore spontaneous heart action.

Comment

The hazards of major operations in patients with hemophilia have been emphasized by Craddock and co-workers[17] and MacFarlane and associates[18] and need not be reiterated here. In the reported case, even though the clotting disorder as assessed in the laboratory was mild, major operation was not performed until it was evident that the patient would surely die without it. Despite the fact that the laboratory tests indicated that the hematological defect was corrected by the administration of fresh frozen plasma and fresh whole blood, it is obvious that adequate hemostasis was not achieved by their administration, even in the doses used.

The treatment of tension pneumothorax was complicated here by the hemorrhagic disorder. Multiple needle aspirations of the chest, which are least likely to cause further bleeding in a hemophiliac, were inadequate to restore a negative intrapleural pressure in this case because of the persistent pulmonary air leak. The immediate respiratory problem was solved by trocar thoracotomy and constant suction. The bleeding was controlled by massive doses of fresh frozen plasma. Prednisone was also used, but its contribution is difficult to evaluate.

The patient's recovery was shortly interrupted by the development of a bronchopleural fistula and an empyema. Because of the persistence of these, despite rib resection and drainage, and because the bleeding defect as measured in the laboratory could be corrected by giving the patient fresh frozen plasma, closure of the fistula and reexpansion of the lung by decortication were elected.

The unavailability of concentrated antihemophilic globulin from animal or human sources led us to use fresh blood and fresh frozen plasma as replacement therapy. The inadequacy of these agents in major hemorrhage has been described by others[18] and was demonstrated by this patient during his early hospitalization and in the period after thoracotomy. It appears that the replacement measures used here can control bleeding in minor procedures, such as trocar thoracotomy or rib resection for empyema drainage. Even in large doses, fresh frozen plasma and fresh blood are inadequate, however, to manage hemophilia in surgery of the magnitude of pulmonary decortication.

It is also apparent that assessment of the level of antihemophilic globulin by the thromboplastin generation test may be deceptive in gauging the severity and likelihood of hemorrhagic complications in hemophilia. A suggestion of the general efficiency of hematological control in minor operations may be gained by a test incision while giving antihemophilic therapy. A precise prediction of the patient's ability to undergo a major operation, however, may be impossible at the present time.

Summary

A case of spontaneous hemopneumothorax occurred in a patient with classic hemophilia. Minor operations—trocar thoracotomy and rib resection—were successfully performed with the use of fresh frozen plasma. The inadequacy of using such conventional replacement therapy for an operation of the magnitude of pulmonary decortication is evident. Preoperative assessment of the operative risk in hemophiliacs by present techniques may be unreliable.

Dr. Joseph McGovern of the Children's Medical Service performed the clotting studies reported.

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COMMITTEE ON COSMETICS

Report to the Committee

The persistent trend toward the incorporation of pharmacologically active ingredients into cosmetics has caused growing concern among the medical profession. One example of this tendency is evident in the increasing interest among cosmetic manufacturers in the possible applications and sales potential of the incorporation of antibiotics into cosmetics. Medical experience provides considerable evidence of the health implications in the widespread, prolonged, or indiscriminate use of antibiotics. Therefore, the Committee has authorized the publication of the following report on the inclusion of antibiotics in products intended for nontherapeutic purposes. VERONICA LUCEY CONLEY, PH.D., *Secretary.*

INCLUSION OF ANTIBIOTICS IN COSMETIC PREPARATIONS

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and
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There seems to be essential agreement that antibiotics generally useful in the treatment of systemic infections should not be used in cosmetics. The risk of sensitization of cosmetic users to such antibiotics could be dangerous. Moreover, and perhaps even more important, the widespread use of cosmetics containing these antibiotics would be unwise because of the possible increased incidence of acquired microbial resistance to such drugs. Therefore, under no circumstances should the antibiotics used in cosmetics include agents of this type.

It has been proposed that agents such as bacitracin, neomycin, polymyxin, and tyrothricin be permitted in cosmetic preparations. Through their use, antimicrobial action would be secured against a wide spectrum of micro-organisms, and the antibiotics used would rarely be required later on for the treatment of systemic infections.

At the present time, the foregoing antibiotics seem to have a relatively low potential for sensitization when applied to the skin. By and large, they are believed not to be potent sensitizers or irritants. Nevertheless, it is not unreasonable to assume that the frequency of sensitization and/or irritation might increase if these agents were applied indiscriminately over a prolonged period of time in an ever-mounting number of individuals. Their use in cosmetics would certainly augment the number of people at risk. By the same token, the time and duration of exposure would inevitably be increased because cosmetics may be applied one or more times each day. We do not have sufficient evidence at this point to state categorically that these compounds cause very little irritation or sensitization of the skin. As time goes on and as the use of these antibiotics becomes more widespread, we may expect that more instances of allergic contact dermatitis, as well as other forms of sensitization and irritation due to these agents, will be reported. Evidence that this may be so is already contained in publications by Baer and Ludwig,[1] Epstein,[2] Sidi, Hincky, and Longueville,[3] and others, including our own observations of isolated cases of allergic contact dermatitis due to neomycin and streptomycin.

In addition, few data are available on the possible toxic effects of bacitracin, polymyxin B, neomycin, and tyrothricin after absorption through the skin. All of these antibiotics are known nephrotoxins. Before they can be legitimately used in cosmetics, evidence should be accumulated to indicate that their prolonged and widespread use on the skin will, in fact, not produce toxic effects of any sort. The burden of proof that such toxicity does not exist rests with those who would include these agents in cosmetics.

Development of Microbial Resistance

A third point at issue in this matter is the possibility that the indiscriminate use of these antibiotics may induce the development of microbial resistance to these agents. Although in vitro studies have indicated that the development of bacterial resistance to these antibiotics is not common, this

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fact should not produce a false sense of security regarding their indiscriminate use. The major result of the widespread use of these antibiotics may be expected to be the elimination of the more sensitive bacterial flora and its replacement by one that is resistant to the action of these agents.

An example of the evidence of this effect can be found in the experience of one of our own institutions. Data accumulated at the Presbyterian Hospital in New York City during the past few years showed an increase in the proportion of antibiotic-resistant micro-organisms isolated from cutaneous infections acquired by the ward population. At the same time, similar infections seen in the outpatient departments of the hospital showed no analogous increase in antibiotic-resistant isolates. Since there was little evidence to indicate that the hospital ward infections were caused by micro-organisms that developed resistance to antibiotics during the patients' hospital stay, the presumption was that these infections were caused by antibiotic-resistant organisms, mainly because their antibiotic-susceptible competitors had been eliminated from the hospital ward environment. It seems, therefore, that the widespread use of antibiotics within a hospital is associated with a disappearance of antibiotic-susceptible organisms, and the strains that remain to produce infections are those that probably were inherently resistant to antibiotics from the beginning. In this connection, it is of interest that the increased percentage of antibiotic-resistant strains of bacteria isolated in the laboratories of Presbyterian Hospital in recent years correlates closely with the increasing extent to which the various antibiotics have been used in the hospital during this period of time.

Although such findings do not conclusively prove that extensive usage is the main factor concerned in changes in resistance of skin bacteria to antibiotics, the inference is that, as antibiotics are used over longer periods of time and with a larger population at risk, the microbial flora found in the environment of that population will be made up more and more of strains of micro-organisms inherently resistant to the antibiotics. Under these conditions, antibiotic-susceptible strains will tend to be eliminated, and it makes little practical difference whether the resistant replacements left free to cause troublesome infections are those that acquire resistance to the antibiotics by their own devices or are those that survive because they are inherently resistant to these agents.

Insofar as we know, there is also no evidence that constant degerming of the skin (except to reduce axillary odors), such as would presumably occur with the widespread use of antibiotics in cosmetics, is necessarily always or even frequently desirable. Evidence has already been presented to show that the widespread topical use of neomycin may increase the number of patients who develop moniliasis as a complication of their therapy.[4] Those who would include such antibiotics as bacitracin, tyrothricin, neomycin, and polymyxin in cosmetics should be prepared to show that their widespread use would not result in an increased incidence of infections due to micro-organisms that are resistant to these agents. Except for the deodorant action of such agents in reducing axillary odors, their incorporation in cosmetics has not been proved to be of specific value, and their widespread use in cosmetics could well represent an increased risk to general public health as well as to certain hypersensitive individuals.

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ADVANTAGES OF GIVING UP SMOKING.—The main advantages of not smoking were wisely summed up by Lord Morton of Henryton in a letter to The Times ten years ago. He had been a heavy smoker for 35 years.... His motive in writing to The Times was not to set forth anti-smoking propaganda, but merely to console people who felt they could no longer afford to smoke. . . . "He who gives up smoking will find," he wrote, "that (1) his general health steadily improves; (2) he plays his favorite game with greater skill and less fatigue; (3) his enjoyment of food and drink is keener; (4) his sense of smell is more acute—this has its disadvantages, but the advantages outweigh them; (5) he no longer has that tiresome cough and his mouth feels cleaner; (6) he saves a lot of money; (7) he has a joyous feeling of independence while others are seeking for cigarettes and matches; (8) he enjoys plays and concerts more because he is not longing for a smoke."—J. H. Doggart, M.D., Smoking as a Factor in Visual Disturbance, *The Practitioner*, February, 1959.

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ORIGIN OF THE TERM "INTERNAL MEDICINE"

GUEST EDITORIAL

Arthur L. Bloomfield, M.D.

RECENTLY Keefer[1] and Rhoads[2] discussed the origin and meaning of the term "internal medicine." They did not bring out, however, what was well known at the turn of the century when German medicine dominated American medical thought, that "internal medicine" is simply a translation of the German *innere Medizin.* We must therefore seek the meaning of the term internal medicine by ferreting out the origin of the German *innere Medizin.*

In looking over the important German treatises on medicine one finds that until the last quarter of the 19th century they were all designated as textbooks of pathology and therapy without any suggestion of the words internal medicine. Felix Niemeyer, in his "Lehrbuch der speciellen Pathologie und Therapie" (Berlin, 1859), says "One will readily discover everywhere [in the book] the scientific striving to apply the newer physiology to the explanation of the pathological and therapeutic facts, and to deduce the symptoms of the illnesses as a necessary consequence." The concept of "internal" medicine was, however, not yet emphasized. Ten years later, in the preface of Niemeyer's seventh edition, Berlin, 1868, there was still no mention of "internal medicine."

But 15 years later the title of Adolf Strümpell's "Lehrbuch der speciellen Pathologie und Therapie der inneren Krankheiten (Leipzig, 1883) has added "of internal diseases," and in the preface he declares that he has tried to bring out "the established facts with reference to internal diseases." What, then, is meant by "internal disease"? All branches of surgery are obviously excluded and the term is clearly used in contrast to external disease, namely, disorders of the skin. Much was made in Germany of dermatology at this time, as witness the numerous treatises of four or more volumes dealing with the subject. Because of the frequent skin lesions of syphilis the dermatologist included syphilis in his domain, and thence extended it to venereal disease in general. There was therefore much for him to do. All this, however, was excluded from the *innere Krankheiten* in distinction to the external diseases—dermatology. It was of course only a short step from internal diseases to the generic term internal medicine and from this to internist as a designation for him who practiced internal medicine.

By 1882 the term was in common use in Germany. So the transactions of the first congress of internal medicine are entitled without further comment "Verhandlungen des Congresses für innere Medicin" (Wiesbaden, 1882). The important journal, *Centralblatt für klinische Medicin* which first appeared in 1881, suddenly changed its name in 1894 to *Centralblatt für innere Medicin.* In the first number of this volume the editor states that this change was made to do away with the misunderstanding that the journal dealt only with purely clinical matters. He said, "our purpose is to give a survey of everything which the world-literature offers in the domain of 'internal medicine.'" Apropos of this point of view J. von Mering in his textbook of internal medicine, "Lehrbuch der inneren Medizin" (Jena, 1901), says "The domain of internal medicine has by the accretion of the most various experimental disciplines reached such a scope that one man can no longer be fully authoritative in all its branches. Only the investigator is competent to critically sift the endless accumulation of detail so that the best can be offered to students and general practitioners." So quite early there was applied to internal medicine a wider concept than that of the simple clinical description of disease; the physiological and chemical basis was included. This concept of "internal medicine" was repeatedly stated by the Germans. The preface to Mohr and Staehelin's monumental "Handbuch der inneren Medizin" (Berlin, 1911) opens as follows: "This book is built up above all on a pathologic-physiological basis." In the second edition (1925) they said "our leading thought is to present 'internal medicine' even more thoroughly on a pathologic-physiologic basis."

From the Department of Medicine, Stanford University School of Medicine, San Francisco.

[1] Keefer, C. S.: What's Ahead for Internal Medicine, New England J. Med. **258**:1087 (May 29) 1958.

[2] Rhoads, P. S.: Internal Medicine and Training of Internists, A. M. A. Arch. Int. Med. **102**:515 (Oct.) 1958.

It is clear then how the concept of "internal medicine" developed in Germany so as to comprise nonsurgical diseases, exclusive of dermatology; the term also implied a scientific attitude quite different from that of the *practischen Arzt*, the general doctor.

In tracing the use of the term in the United States, one must remember the immense influence of German medicine on ours before World War I. Doctors in huge numbers went to Germany to study; microscopes, instruments, and laboratory glassware were imported from Germany; one did not do a research, one did an *Arbeit*; one did not speak of laboratory assistants, one spoke of the *Diener*. Small wonder then that many expressions were simply translations of the German. The word, "Archives" is simply a translation of German *Archiv*. The English use of the term, however, is absurd, since it is a place to keep records and presumably should be used for dead storage and not for new material. So dominated by German thought was American medicine that the *Archives of Internal Medicine* was launched in 1908 without a word of prefatory material. Forchheimer's well-known book, "The Prophylaxis and Treatment of Internal Diseases" (New York, 1906), evidently was copied from the German *innere Krankheiten*. So too we have through the years such textbooks as Musser's "Internal Medicine" (Philadelphia, 1932) and Yater's "Fundamentals of Internal Medicine" (New York, 1954). The American Medical Association nevertheless did not replace its section on the Practice of Medicine by one on Internal Medicine until 1945.

In Britain things are different. Although much closer to Germany, British medicine shows little evidence of German influence. To my knowledge, the term "internal medicine" is not used in England. There is no textbook on "internal medicine" nor is there a journal with "internal medicine" as part of the title.

So whatever implications may now be attributed to it, the origin of the term "internal medicine" is quite clear.

NOISE OF JET ENGINES MAY BE A HAZARD

While progress in aviation provides greater speed in travel and comfort, it introduces a noise hazard which if not recognized and understood can cause deafness. Until recently the noise of jet engines has been a problem associated primarily with the military air bases and experimental airfields of plane manufacturers. Since commercial aviation has entered the age of jet powered aircraft, the noise of jets will have some effect on many other persons, such as travelers, crew members, and ground personnel. Probably several million persons living very near airports will notice differences between the noise of jet aircraft and that of conventional propeller airplanes. Although these persons may complain of the noise, they are not likely to be deafened because the sound intensity will be lower than the hazardous levels.

Several thousand persons in the United States work at airports. The so-called ramp personnel, those who work outside and inside the terminal buildings and the operators in maintenance areas of airports, will at times be working in dangerous sound levels. In an article "Airports and Jet Noise,"[1] Miller, Beranek, and Kryter show that the sound-pressure levels 100 ft. from the center of the four-jet engine array during warm-ups and ramp operations may be as much as 110 db. This condition is not desirable, especially if a person is exposed to such noise intensity for long periods. If a person, attendant, or passenger should get nearer than 100 ft. the noise can cause injury to the ear.[2] The ramp attendants and service crews are required to use noise reduction ear plugs and ear muffs during the engine run-ups and other ground operations. When the jet engines are being serviced they are placed in acoustically treated test cells to protect the mechanics and to reduce the noise radiated to nearby residential areas. Reliable evidence indicates that passengers emplaning or deplaning will not be subject to hearing trauma. The occupants in the fuselage of the plane are also protected. If, however, a passenger or a helper should step too close to the exhaust of the jet engines, an injury within the ear could occur. Because people vary in their response to loud noises, the maximum safe noise-intensity level cannot be stated as a single over-all value. If a worker or passenger comes near the exhaust stream of a jet engine, as much as 120 db. in the 150 to 300 cycles per second band can be impressed on an unprotected ear. This is a dangerous sound intensity level.[2] Prolonged exposure to noise (in the 300 to 600 or 600 to 1,200 cycles per second bands) of the order of 85 db. suggests initiation of a noise-exposure control program and tests of hearing for those exposed to this noise.[3]

All physicians might well inform themselves about this hearing hazard which is an unfortunate by-product of progress in air travel.

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1. Miller, L. N.; Beranek, L. L.; and Kryter, K. D.: Airports and Jet Noise, Noise Control 5:24-31 (Jan.) 1959.
2. Industrial Noise Manual, Detroit, American Industrial Hygiene Association, April, 1958.
3. Guide for Conservation of Hearing in Noise, Subcommittee on Noise in Industry, Committee on Conservation of Hearing, American Academy of Ophthalmology and Otolaryngology, Noise Control 3:23-31 (May) 1957.

ORGANIZATION SECTION

THE EMBLEM OF THE AMERICAN MEDICAL ASSOCIATION

George M. Fister, M.D., Ogden, Utah
and
Thomas A. Hendricks, Chicago

The gods of mythology, Mercury, Aesculapius, Zeus, Pluto, and others probably will shudder in their retreats to find another human writing about the caduceus. Many humans probably will be equally amazed at this attempt to clarify a confusion that has developed out of the simplicity of the gods' intentions.

The gods' intentions were probably very clear, but between the ancient Greeks, the slightly less ancient Romans, and modern physicians there has developed ambiguity and uncertainty about the emblem of medicine.

By definition the word caduceus is a Latin adaptation from the Greek, a herald's wand (kerykeion), so the only meaning that the word caduceus has is a herald's wand. It has no connection with and carries no implication as a symbol of medicine. The herald who carried the wand (the caduceus) was the Greek god Hermes, also referred to as Mercury by the Romans.

Now Hermes was quite a god of classical mythology. He was a messenger, a herald of assemblies, the patron of commerce and peace, god of the rogues, and was undoubtedly a clever thief and could roll a wicked game of dice. It would seem that he didn't have enough to do, so he was further assigned the duty of conductor of the souls of the dead to the infernal regions. Hermes was no doubt as fluid and as slippery as the metal called mercury.

It was clear that no herald could function without a wand; to do so would have been as impractical as a chairman without a gavel. So Hermes immediately secured for himself a straight piece of an olive tree branch which was used as his wand. Thus the herald's wand, or caduceus, became one of Hermes' sacred possessions and he was apparently seldom seen without it.

The transition from the simple herald's wand to the more elaborate one with two snakes entwined was probably a gradual process, the addition of the snakes having been inspired by various legends plus the artists' interpretations. One legend relates that Hermes found two snakes fighting with each other. Hermes separated them with his olive branch wand, and by his kindness and the snakes' appreciation, they entwined themselves on his wand. Since Hermes was the messenger of the gods, two wings were added to the wand. These perhaps were to give him an increase in speed as he carried messages between friends and enemies. Thus Hermes, with the caduceus, became an emblem of commerce and perhaps neutrality.

A review of the literature permits and sustains the conclusion that the caduceus was simply the herald's wand of the winged god Hermes and was (and still should be) an emblem of all of his numerous duties, which did not include medicine.

According to Arnold [1] "All the meanings that we might attach to the caduceus can be summed up into one: vis; that it symbolizes the peaceful condition of business—the mercantile world as opposed to the military." Nevertheless, the U. S. Army Medical Corps and the U. S. Public Health Service continue to use the emblem of Hermes as their insignia. Probably its use here is justified, the intent being to portray the noncombatant character of the Medical Corps rather than as an emblem of the medical profession. In addition, the name caduceus is used almost universally, except in England, France, and Germany, as the emblem of the medical profession, an error that seems impossible of correction, but one that merits our best efforts to correct.

What then is the true emblem of the American Medical Association? Mythology relates that the Greek god Asklepios (Roman Aesculapius) [2] "studied the healing art and soon surpassed his teacher (Chiron) for his patients never died and he even succeeded in recalling the dead." Thus Asklepios was recognized by the Greeks as the god of medicine. Up to this point there is no apparent confusion between the two, Hermes and Asklepios, but for professional reasons Hermes carried a wand and Asklepios carried a staff and each began association with snakes. Complication of the significance of the symbols was the immediate result.

It is quite likely that Hermes and Asklepios sensing the need for a cane or walking stick, each unknown to the other, picked up a branch. Hermes made a straight olive wand, while Asklepios, being a little more rugged, made a knotty pine staff. Then along came the serpent! Like any physician, Asklepios was satisfied with and perhaps could afford only one, but Hermes, trained in the ways of commerce, sought out two snakes. The snakes in each case followed their natural instincts and entwined themselves about the sticks, one on Asklepios' staff and two on Hermes' wand.

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Thus we have two symbols, the caduceus, a wand entwined with two serpents, and the staff of Asklepios, entwined with one serpent. Asklepios was recognized by the Greeks as god of medicine. His fame spread throughout the Mediterranean area and he is reported to have had many medical sanctuaries, one of them in Epidaurus near Athens. Medical therapy in the era of Asklepian temple healing, extending into the third century A. D., must have been impressive if not always curative for Asklepios is reported to have had a large following, what we would now refer to as a successful practice.

Of course Asklepios, the Greek physician, did not wear a stethoscope, but he was always seen with his heavy staff. After his death he was worshiped as a god by the Greeks and Romans. Mythology relates the origin of his birth, and his death was the result of Pluto's jealousy, who had Jupiter destroy him with a thunder bolt, which seems to be a noisy way the ancients had of removing any competition. Many shrines were built in honor of Asklepios, the god of health, where was carried on a special type of healing by incubation.

Serpents since the time of Adam have been regarded with both fear and admiration. The snake's annual renewal of its skin, the graceful movements, its speed and destruction of its prey gradually led to sacred fascination and worship. To the snake was attributed rejuvenation, convalescence, wisdom, and long life. The serpents soon participated in certain rituals that were a definite part of the healing and curative procedures in the Asklepian temples. In recognition the staff of Asklepios became adorned with a serpent, a symbol of the medical profession.[3] "Reproduction of the statues of Asklepios usually show the physician standing in flowing toga with his right hand clasping the staff, along which a single snake makes its way upward." There need be no uncertainty about who is the mythical Greek and Roman god of the art of medicine. All legends, documents, and statues point definitely to Asklepios.

The American Medical Association in 1910 by official action of the House of Delegates adopted a report by a committee that had been appointed to revise the emblem of the Association. The Committee stated "The true ancestral symbol of the healing art is the knotty pine and the serpent of Asklepios. That the color of the new emblem should be scarlet and gold and the new emblem should be the knotty rod entwined with the serpent."[4] Much credit is due the Committee that was assigned to this task.

In retrospect of the error and looking forward to its correction, the following summation is presented: 1. The word caduceus means a herald's wand. It is a straight wand entwined with two serpents. It is not an emblem of the medical profession (although it has been adopted by medical and lay organizations). 2. Asklepios was a medical deity or legendary physician and he was enshrined as the mythical god of medicine. 3. The emblem of the American Medical Association is the knotty staff of Asklepios, entwined with one serpent. This is not a caduceus and should not be confused with one or referred to as one. 4. The American Medical Association should conduct an educational program to correct the grossly negligent use of the word caduceus. State, county, and local medical societies should assist the program. All physicians should be made acquainted with the emblem of the American Medical Association, which is the staff of Asklepios (Roman Aesculapius).

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2. Veith, I.: Symbol of Medicine: Caduceus of Hermes or Knotted Staff of Aesculapius? **26:**138-148 (July 15) 1958. Zwick, K. G.: Origin and Significance of Medical Emblem, Bull. Soc. M. History, Chicago **4:**94-105 (April) 1928. Bremer, L. J.: Caduceus Again, New England J. Med. **258:** 334-336 (Feb. 13) 1958. Tobey, J. A.: Magic Wands of Medicine, Hygeia **8:**348-350 (April) 1930.

3. Stenn, F.: Personal communication to the author.

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REPORT OF JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

The following items from the March, 1959, issue of the bulletin of the Joint Commission on Accreditation of Hospitals (660 N. Rush St., Chicago; Kenneth B. Babcock, M.D., director) are presented for the information they contain that will be of interest to many physicians.—Ed.

Report of Activities of Accreditation Commission for 1958

As of Dec. 31, 1958, there were 3,896 hospitals on the Joint Commission on Accreditation of Hospitals list (3,523 in the United States, 2 in the Canal Zone, 22 in Puerto Rico, 16 in Hawaii, 323 in Canada, and 9 in other countries). In 1958, the cost of a survey averaged $175.14. This figure does not include the sums spent by the American College of Surgeons and the American Hospital Association for overhead expenses of maintaining field staffs. If these were included, the cost per survey would be much more. Because of this monetary cost and the loss of precious time, the Commission is reluctant to cancel or postpone a scheduled survey. It is rare that another survey can be substituted for a cancellation, so time is lost and expenses go on. It sometimes happens that a hospital seeking accreditation for the first time cancels its survey when it is scheduled. The reason given is that the hospital is not yet ready and asks for more time to prepare for the survey. This procedure is costly and should be avoided. A request for accreditation should not be made until the hospital is willing to have a survey. The Certificate of Accreditation is being revised. This is necessary because of the resignation of the Canadian Medical Association. This is taking longer than anticipated, so the certificate for those hospitals accredited since Jan. 1, 1959, will be delayed.

Canada Launches Its Own Accreditation Program

On Jan. 1, 1959, the Canadian Council on Hospital Accreditation assumed the responsibility of accrediting hospitals in Canada. To give its full support to this program, the Canadian Medical Association resigned its membership in the Joint Commission on Accreditation of Hospitals. Motivated by an admirable spirit of national independence, the organization of the Canadian Council marks the culmination of several years of working and planning. Its members are the Canadian Hospital Association, the Canadian Medical Association, the Royal College of Physicians and Surgeons of Canada, and L'Association des Medecine de Langue Francaise du Canada. The aim of the program is the same as that of the Joint Commission on Accreditation of Hospitals, namely to help improve the quality of care rendered to patients in hospitals. There will be little or no departure from the program established by the American College of Surgeons and the Joint Commission on Accreditation of Hospitals. The standards for hospital accreditation of the Commission have been adopted by the Council as a basis for accreditation, as well as the survey procedures and report forms.

In order to give full support to the Canadian program, the Joint Commission on Accreditation of Hospitals has agreed to discontinue surveying and accrediting hospitals in Canada. This does not mean that the Commission is less interested in Canadian hospitals, but rather that the Commission will do everything possible to help the Canadian program succeed. Effective liaison will be established on both governing and administrative levels and efforts will be made to keep both programs as much alike as possible.

Representation on the Board of Commissioners Changed.—With the resignation of the Canadian Medical Association, the members of the Joint Commission on Accreditation of Hospitals voted that representation on the Board of Commissioners will be as follows:

American College of Physicians	3 votes
American College of Surgeons	3 votes
American Hospital Association	7 votes
American Medical Association	7 votes

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

Strontium-90 Fall-out.—There is nothing good about radioactive fall-out, and a constant effort is being made to reduce it to the minimum. A comprehensive document (Health and Safety Laboratory Report No. 42, Environmental Contamination from Weapons Tests) issued recently gives a nearly complete summary of U. S. data up till about last summer. It is available through the Department of Commerce Office of Technical Services. The high levels found sometimes in wheat, rice, other grasses, and various vegetables apparently are due to the fact that these plants pick up more fall-out from the rain falling directly on the leaves than from the roots and the soil. As a consequence their level depends more on the rate of fall-out than on the total accumulated fall-out in the soil, though there definitely is some pickup from the soil. The soil pickup, however, does not lead to the large fluctuations with seasons of the year that are found in these grasses and remains at lower values than the peaks that direct leaf pickup can attain during a period of intense nuclear weapons testing when the rate of fall-out can be particularly high for a short time. The amount of strontium-90 found in these products at times exceeds the levels considered acceptable for a steady diet. The general average food level, however, is the important figure and this is well below the maximum permissible level as given by the National Committee on Radiation Protection.

PUBLIC HEALTH SERVICE

Personal.—Dr. Robert C. Berson, vice-president of the University of Alabama Medical Center in Birmingham; Dr. E. Dwight Barnett, director of the Palo Alto–Stanford Hospital Center in Palo Alto, Calif.; Dr. Owen H. Wangensteen, chief of the Department of Surgery at the University of Minnesota Medical School, Minneapolis; and Dr. Thomas B. Turner, dean of the Medical Faculty of the Johns Hopkins School of Medicine in Baltimore, Md., have been appointed members of the National Advisory Council on Health Research Facilities. This is a reappointment for Dr. Turner. These doctors will advise and make recommendations to the surgeon general on matters relating to the federal program to strengthen the nation's capacity for medical research by constructing and equipping health research facilities.

MEDICAL NEWS

ALABAMA

Annual Session in Birmingham.—The Medical Association of the State of Alabama will hold its annual session in Birmingham April 9-11, with headquarters at the Dinkler-Tutwiler Hotel and with Dr. Edgar G. Givhan Jr., president of the association, presiding. Dr. S. Joseph Campbell, president, Jefferson County Medical Society, will present an address at the opening business meeting. The scientific program will include the following papers by out-of-state speakers:

Practical Shortcuts in Endocrinology, Diagnosis and Treatment, Dr. Peter H. Forsham, San Francisco.
The Diagnostic Value of Intravenous Cholangiography in Biliary Tract Disorders and Acute Abdominal Conditions, Dr. H. Stephen Weens, Atlanta, Ga.
Dietary Management of Children in Illness and in Health, Dr. Frederic G. Burke, Washington, D. C.
Pruritus Vulvæ, Dr. J. Donald Woodruff, Baltimore.
Prenatal Care—The Pale Pink Pill, Dr. Lawrence L. Hester Jr., Charleston, S. C.

The Jerome Cochran Lecture, "Somatopsychic Medicine," will be given April 10 by Dr. Sara M. Jordan, Boston. Dr. Louis M. Orr, Orlando, Fla., President-Elect, American Medical Association, will present "Medical Show Window of the World," and Mr. Leo Brown, Director, Communications Division, A. M. A., will speak on "The Second Mile." The presidential dinner-dance April 10 will be held at the Vestavia Country Club. For information, write Mr. W. A. Dozier Jr., 19 S. Jackson St., Montgomery 4, Ala., Executive Secretary.

CALIFORNIA

Study of Altitude Effects on Newborn.—To study effects of altitude on the hearts of newborn babies, Dr. Herbert N. Hultgren, head of Stanford's Cardiovascular Research Laboratory, made a trip to the Andes of South America under a grant from the National Heart Institute, U. S. Public Health Service. His headquarters were a hospital in La Oroya, Peru (altitude, 12,500 ft.). He carried a portable electrocardiograph, but the remainder of his equipment was furnished by the hospital at La Oroya. Dr. Hultgren plans to survey the potential for more extensive studies in the future.

CONNECTICUT

Annual State Meeting in Hamden.—The 167th annual meeting of the Connecticut State Medical Society will be held in Hamden High School, Hamden, April 28-30. The House of Delegates will meet April 28, with Dr. Thomas M. Feeney, Hartford, speaker of the house, presiding. Eleven sectional meetings of society and guest organizations are planned for the afternoon of April 29, with the annual dinner scheduled for that evening. The following papers will be presented by out-of-state speakers:

Multiple Antibiotics—Use and Abuse, Dr. Monroe J. Romansky, Washington, D. C.
Chemotherapy of Cancer in Children, Dr. Sidney Farber, Boston.
The Place of Serum Enzyme Determinations in Diagnosis and Treatment, Dr. John S. LaDue, New York City.
The Problem of Chronic Pancreatitis, Dr. Kenneth W. Warren, Boston.
The Use of Enzymes and Anti-Inflammatory Drugs in Surgical Disease, Dr. Eugene E. Cliffton, New York City.
Management of the Patient with Peripheral Obliterative Arterial Disease, Dr. Robert R. Linton, Brookline, Mass.
New Trends in Management of Diverticulitis, Dr. Alfred S. Frobese, Philadelphia.
Diagnosis of Vulvar Lesions, Dr. Mortimer D. Speiser, New York City.

A symposium, "Upper Gastrointestinal Hemorrhage," will be conducted the afternoon of April 30, with Dr. Paul D. Rosahn, New Britain, as chairman. For information write the Connecticut State Medical Society, 160 St. Ronan St., New Haven 11, Conn.

DISTRICT OF COLUMBIA

Dr. Head Admitted to Virginia Bar.—Dr. E. Murdock Head, of the surgical department, George Washington University Hospital, was recently admitted to the Virginia Bar and to practice before the Court of Appeals of Virginia. Dr. Head has, in addition to his M.D., degrees in dentistry and law. He is primarily interested in the teaching of legal-medicine.

Personal.—Dr. Edward D. Freis, associate professor of medicine, Georgetown University School of Medicine, was recently elected vice-chairman and chairman-elect of the Council on High Blood Pressure Research of the American Heart Association. ——Dr. Ralph M. Caulk was reelected president of the medical staff of the Washington Hospital Center at a meeting March 2.

Dr. Hufnagel Gives Kober Lecture.—Dr. Charles A. Hufnagel, professor of surgery and director of the Experimental Surgery Laboratory at the Georgetown University School of Medicine, delivered the 1959 Kober Lecture at Georgetown University

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

March 11 on "The Basic Concepts of Cardiac and Vascular Reconstruction." The Kober Lecture is provided for by the Kober Foundation of Georgetown, established by the late Dr. George M. Kober, dean of the university's Medical School from 1900 to 1929. Dr. Hufnagel was selected for this year's honor by the executive committee of the Medical Society of the District of Columbia.

FLORIDA

Civic Advisory Council for School Development.—Creation of a new advisory council of civic leaders for the School of Medicine of the University of Miami was authorized by the trustees of the university. Mr. Hoke Maroon, president, Merchants Bank of Miami, was named temporary chairman of the new group. In outlining the responsibilities of the new council, Jay F. W. Pearson, Ph.D., president of the university, indicated that it would concern itself with institutional and financial development of the medical school and all phases of the school's operation touching on the public interest. The council will be responsible to the university board of trustees and, when fully formed, will consist of 21 civic leaders, of whom about one-fourth will be physicians. Subcommittees of the council will deal with institutional development, financial development, and community relations.

IOWA

Annual Meeting in Des Moines.—The 1959 annual meeting of the Iowa State Medical Society, organized in 1850, will be held April 19-22 in the Veterans Memorial Auditorium, Des Moines. The president's address will be given by Dr. Walter D. Abbott, Des Moines. Dr. Ralph M. Kniseley, Castro Valley, Calif., will give the Arthur Erskine Memorial Lecture, "Important Non-Biological Contributions to Radioisotopic Diagnosis," April 21. Papers by out-of-state speakers include:

Aneurysms and Occlusive Disease of the Aorta and Peripheral Arteries: Experience with 2,000 Cases, Dr. George C. Morris Jr., Houston, Texas.
The Growth Pattern of Endometriosis, Dr. Roger B. Scott, Cleveland.
Respiratory Obstruction in Infants, Dr. F. Johnson Putney, Philadelphia.
Pediatric Urology, Dr. Robert Lich Jr., Louisville, Ky.
The Role of the Family Physician in Congenital Heart Disease, Dr. Patrick A. Ongley, Rochester, Minn.
Child Psychiatry for the General Practitioner, Dr. Reynold A. Jensen, Minneapolis.
Factitial Enteritis: An Unusual Cause of Intestinal Obstruction, Chronic Blood Loss, or Malabsorption Syndrome, Dr. William G. Sauer, Rochester, Minn.
The Place of Radioactive Isotopes in the Community Hospital, Dr. Frank R. Hendrickson, Chicago.
Problems Involved in the Treatment of Injuries to the Central Nervous System, Dr. Winchell M. Craig, Rochester, Minn.

Symposiums on "Exfoliative Cytology" and "Clinical Uses of Radioisotopes" are planned. Dr. Gunnar Gundersen, LaCrosse, Wis., President, American Medical Association, will present "Keeping the Paths Open" April 22. Scientific and technical exhibits and special meetings and dinners are arranged. The annual golf tournament will be held April 19, and the annual banquet, April 21, 7 p. m. The scientific program is acceptable to the American Academy of General Practice for 12 hours credit in category II.

KENTUCKY

Report on Diabetes Detection Drive.—One hundred eighty newly proved diabetics were discovered in Kentucky during the 1958 Diabetes Detection and Education Drive sponsored by the Kentucky State Medical Association in November, Dr. Robert J. Hoffmann, South Fort Mitchell, chairman, KSMA's Associate Committee on Diabetes, has announced. More than 90,500 Kentuckians in 72 counties were tested free of charge during the drive, according to the latest reports. Of these, 1,166 were found to have positive urine sugars. Final figures in the previous drive in 1957 indicated that 52,400 were tested in 83 counties and 137 newly proved diabetics were discovered.

LOUISIANA

Pediatric Meeting Features British Physician.—The Baton Rouge Pediatric Society announced that its June 16 quarterly meeting will consist of a program by Dr. Alan A. Moncrieff, chief of staff, The Hospital for Sick Children, Great Armond Street, London, England. The subject will be "Biochemistry and Mental Defects." For information write Dr. Francis M. Harris Jr., Secretary-Treasurer, Baton Rouge Pediatric Society, 1401 N. Foster Dr., Baton Rouge, La.

University News.—Dr. Alvar P. Wilska, of Helsinki, Finland, was appointed visiting professor of cell research at the Louisiana State University School of Medicine, New Orleans. Dr. Wilska will continue his work on the new electron microscope and inaugurate additional research projects in the department of anatomy with Frank N. Low, Ph.D., university professor and director of the electron microscope laboratory at Charity Hospital. A graduate of Helsinki University, Dr. Wilska received a degree of doctor of medicine and surgery in 1938 and served there as professor of physiology since 1944. He assumed his new duties Jan. 5.

MARYLAND

Annual Meeting in Baltimore.—The Medical and Chirurgical Faculty of Maryland will hold its 161st annual meeting April 15-17 at the Alcazar, Baltimore. Four illustrated papers will be given the afternoon of April 15:

Surgical Treatment of Aortic Valvular Disease, Dr. Charles A. Hufnagel, Washington, D. C.

Leukemia: Present Status, Dr. William Dameshek, Boston.
Surgical Treatment of Chronic Pancreatitis (J. M. T. Finney Fund Lecture), Dr. Ralph F. Bowers, Memphis, Tenn.
Atherogenesis and Lipid Metabolism, Dr. Charles F. Wilkinson Jr., New York City.

Dr. J. Sheldon Eastland, president of the faculty, will preside at a medicolegal symposium, "Whiplash Injuries: A Conference Between the Counsel and Medical Witnesses." The William Royal Stokes Memorial Lecture will be given by Dr. Horace L. Hodes, New York City, on "Staphylococcal Infections in the Antibiotic Era." Panel discussions on adrenocortical steroid therapy and on therapeutic uses of radioiodine are planned. The I. Ridgeway Trimble Fund Lecture, "Lesions of the Adrenal Glands (Illustrated)," will be presented by Dr. James T. Priestley, Rochester, Minn., April 16, to be followed by Dr. Edgar V. Allen, Rochester, Minn., presenting "The Natural History of Arteriosclerosis Obliterans (Illustrated)." Milton S. Eisenhower, president, Johns Hopkins University, Baltimore, will speak on "Our Partnership with Latin America" at a general meeting April 16, following the presidential dinner ($6.50). Round-table luncheon discussions (April 16) and exhibits are planned. Twelve hours category I credit will be given by the American Academy of General Practice for attendance. For information write Mr. John Sargeant, 1211 Cathedral St., Baltimore 1, Md., Executive Secretary.

MICHIGAN

Annual Conference on Aging.—"Designs for Retirement" will be the theme of the University of Michigan's 12th annual Conference on Aging June 22-24 in Ann Arbor. Over-all plan for the conference calls for five separate groups to meet simultaneously. Topics covered will include retirement health, retirement housing, retirement financing, retirement preparation, and uses of retirement. For information on the conference, write the Director, Wilma Donahue, Chairman, U-M Division of Gerontology, 151 Rackham Building, Ann Arbor, Mich. On June 24-26, immediately following the conference, the U-M will host a National Leadership Training Institute for the White House Conference on Aging. The institute is sponsored by the U. S. Department of Health, Education, and Welfare in cooperation with other interested federal agencies and the university.

Health Survey of Tecumseh.—Individual physical examinations for more than 8,000 residents of the Tecumseh area are scheduled as a result of a two-year grant of $280,000 given to The University of Michigan School of Public Health by the National Heart Institute, a branch of the U. S. Public Health Service. Researchers plan to make a complete health survey of each individual, but will seek special details on heart disease and related disorders. Each person will be notified of the results of his examination, and detailed medical reports will go to family physicians. The total body of data will be used to create a comprehensive picture of sickness and health in a single community. Dr. Thomas Francis Jr., who directed the nationwide field trials of the Salk polio vaccine, and Dr. Frederick H. Epstein are in charge of the survey. It is part of a broader community study directed by Dr. Robert J. M. Horton. All are faculty members of the University of Michigan School of Public Health.

MISSISSIPPI

New Department of Clinical Laboratory Science.—The University of Mississippi School of Medicine, Jackson, has created an independent department of clinical laboratory science, with Dr. Warren N. Bell as its chairman. The new department was formerly a division in the department of medicine, and Dr. Bell retains his appointment as an associate professor of medicine in addition to his new chairmanship.

MONTANA

Interim Meeting Held in Helena.—The 12th interim session of the Montana Medical Association was held April 3-4 in the Western Life Insurance Company Building, Helena, with Dr. Herbert T. Caraway, president of the association, presiding at the morning session April 3. Four panel discussions were held, with the following titles and moderators:

The Use and Disuse of ACTH and Adrenocorticoid Drugs, Dr. George B. LeTellier, Lewistown.
The Business Side of Your Profession, Mr. Norman McGinty, Billings.
Treatment of Acute Multiple Injuries, Dr. Warren H. Randall, Miles City.
Clinical Pathological Conference, Dr. Bernard J. Winter, Billings.

Three motion pictures were shown, and a tour of the State Board of Health Laboratory was held. At the banquet April 3, Dr. Everett H. Lindstrom, Helena, was the toastmaster.

NEW JERSEY

State Convention in Atlantic City.—The 193rd annual meeting of the Medical Society of New Jersey will be held April 25-29 in Haddon Hall, Atlantic City. An open "Discussion on Medical-Surgical Plan" will follow the Golden Merit Award ceremony April 25, and the House of Delegates will meet April 25, 26, and 27. Over 15 section meetings will be held April 28 and 29, with the following symposiums included:

Bronchial Asthma as an Occupational Hazard (Allergy).
Which of Your Patients Can Now Be Benefited by Cardiac Surgery? (Cardiovascular Diseases).

Diarrhea (Gastroenterology and Proctology).
The Prevention of Perinatal Loss (Obstetrics and Gynecology).
Certain Aspects of Eye Care in Children (Ophthalmology and Pediatrics).

At the general practice session, Drs. Milton Jabush, Lakewood, Abraham Weinberg, New York City, and Jacob H. Conn, Baltimore, will present "The Use of Hypnosis in Obstetrics," "Hypnosis in General Practice," and "Medical Hypnosis, Its Use and Abuse," respectively. Motion-picture theaters, special luncheons, and scientific and technical exhibits are planned. The Doctors' Chorus of the Essex County Medical Society will entertain at the dinner-dance April 28, 7 p. m. For information write the Medical Society of New Jersey, 315 W. State St., Trenton 8, N. J.

NEW YORK

Increase in Rabies in 1958.—The number of laboratory confirmed cases of rabies increased in the state in 1958. During the year, a total of 261 cases was reported to the Bureau of Epidemiology and Communicable Disease Control, New York State Department of Health, compared with 202 cases in 1957. Dr. Herman E. Hilleboe, state health commissioner, stated that the number was 55 less than that reported for 1956, however. Rabies was reported in 26 counties, being most prevalent in the following: Otsego, 65 cases; Delaware, 46; Chenango, 28; Madison, 23, and Steuben, 21. A total of 146 cases was reported in cattle. Other cases included dogs, 21; foxes, 56; cats, 21; raccoons, 7; sheep, 5, and horses and bats, two each. Dr. Hilleboe said that in recent years the reported incidence of rabies has been cyclic in nature with peaks of decreasing magnitude occurring every three or four years, starting with the peak incidence of 1,155 cases reported in 1946.

Study of Gamma Radiation.—An aerial survey to determine existing gamma radiation for an area of New York State, reportedly the first to be conducted by a state health department, was completed in the Hudson Valley area. Dr. Herman E. Hilleboe, State Health Commissioner, said establishment of existing gamma radiation levels makes it possible to compare preoperational and operational gamma levels for the area in the vicinity of atomic power plants. The survey was made in a helicopter provided by the Department of Defense. Five counties in the Lower Hudson River Drainage Basin are included in an environmental radiation survey being conducted by the State Health Department in cooperation with local health departments and the State Conservation Department. The others are Dutchess, Orange, Putnam, and Rockland. It is expected that by 1960, three nuclear reactors will be in operation in the Lower Hudson River Drainage Basin. The results of the aerial survey are being coordinated with the over-all sampling and spot checks in this area. When the preoperational aerial survey was made, the major contributing factors to gamma-ray emissions recorded included: cosmic radiation, natural radium and daughter products in the soil, rock, and vegetation, daughter products of radon in the air, natural potassium-ro in the soil, rock and vegetation, and particulate air matter and absorbed fission products on the ground resulting from the continuous fallout of fission products associated with nuclear test devices.

New York City

Physicians' Wives Hold Dinner-Dance.—Physicians and their wives of Greater New York are invited to attend a dinner-dance, sponsored by the Physicians' Wives League of Greater New York, to be held April 5 at the Waldorf Astoria Hotel. The league works to aid indigent physicians and their families. For information, write Mrs. Louis Wexler, 5 E. 76th St., New York 21.

Triplets Exceed Statistical Expectations.—More than three times as many triplets have been born in New York City so far this year as were statistically expected. There were 10 sets of triple births since the first of the year, Carl Erhardt, director of the Bureau of Records and Statistics, New York State Department of Health, announced March 8. Three sets of triplets were expected because vital statistic records show that triple births usually occur once in 9,900 deliveries. Since there have been 28,000 births so far this year, three sets of triplets was the statistical expectation. Instead of three sets among these 28,000 births, there were 10. Of the 30 babies in these 10 sets of triplets, 4 died at birth, 26 lived. Among the 167,775 births which occurred in 1958, there were 15 sets of triplets. Of these 45 infants, three died at birth, 42 lived. The triple births by boroughs were:

	1958	1959
Manhattan	4	1
Bronx	2	–
Brooklyn	4	5
Queens	5	2
Richmond	–	2
	15	10

Dr. Cooper Cited by Hospital.—Dr. Irving S. Cooper, director, department of neurosurgery, St. Barnabas Hospital for Chronic Diseases, Bronx, was honored by the hospital's board of managers at their 93rd annual meeting. Dr. Cooper, who developed the chemopallidectomy and who is professor of research surgery and director of the division of neuromuscular diseases at New York University Postgraduate Medical School, was awarded a citation by St. Barnabas Hospital in recognition of "distinguished leadership and outstanding contributions to medical science and to the professional services of St. Barnabas Hospital in the field of neurosurgical research and the treatment and alleviation of extrapyramidal disorders." As part of the ceremonies, a 27-minute sound film was shown.

Survey of Orthopedic Ailments in Children.—A youth health survey, in which 600 presumably normal children, age 10 to 14 years, from the Sen. Robert F. Wagner Junior High School in Manhattan were examined for unsuspected orthopedic ailments, was completed at the Hospital for Joint Diseases March 6 after 4½ months of work. The study was undertaken under the auspices of the Board of Education, the Department of Health, and the Hospital for Joint Diseases, a voluntary, nonprofit hospital located at 123rd Street and Madison Avenue. The hospital reported finding a considerable number of children with orthopedic difficulties of some kind, many of them previously unsuspected. Most of these ailments were minor, requiring corrective exercises, but a few serious conditions, resulting from "growth disturbances," were noted. All abnormalities found were promptly reported by the hospital to the principal of Robert F. Wagner Junior High School and to the Department of Health's Bureau of School Health, so that the parents could be alerted to bring their children under treatment. Robert F. Wagner Junior High School was chosen for the study by a joint hospital, Board of Education, and Department of Health committee because the students were deemed to constitute a representative cross-section of the city's school population in the 10-14 age bracket. The examinations have been conducted at the hospital's orthopedic clinic every Friday afternoon since Oct. 24, 1958, under the supervision of Dr. Michael S. Burman, attending orthopedic surgeon.

NORTH CAROLINA

Plan Building for Aging Study.—Plans for a building to house the Duke University Regional Center for the Study of Aging were announced by Duke President Hollis Edens. The structure will provide facilities for a multipronged attack on the problems of aging by researchers in medical, biological, social, and behavioral sciences. A construction grant of $388,000 was made to Duke by the National Institutes of Health, research center of the U. S. Public Health Service. Matching funds, now being sought by the university, will bring the total to $776,000. Preliminary plans call for the building to be erected in front of Duke Hospital where a parking area is now located near the hospital emergency entrance. The structure will be of modified Gothic architecture and will be faced with native North Carolina stone to match other West Campus buildings. Some 35,000 square feet of floor space will be provided by five stories, including a basement and sub-basement. Dr. Ewald W. Busse, Duke psychiatry department chairman, is head of the Regional Center for the Study of Aging. Representing a concentration of University-wide interest in this field, the center was established in July, 1957, with U. S. Public Health support which will total $1,500,000 over a five-year period. The Ford Foundation recently augmented these funds with a $200,000 grant for a sociological-economic study in aging.

OHIO

Dr. Griffith to Give Annual Lecture.—Dr. Harold R. Griffith, emeritus professor of anesthesia, McGill University, Canada, will be the guest speaker at the third annual Rolland J. Whitacre Memorial Address, sponsored by the Cleveland Society of Anesthesiologists. His talk, entitled "Adventures and Misadventures in Forty Years of Anaesthesiology," will be given at a dinner meeting at the Tudor Arms Hotel, Cleveland, the evening of May 20. For reservations, write Dr. Sidney W. Helperin, 20665 Centuryway, Maple Heights 37, Ohio.

Personal.—Dr. Robert J. Izant Jr. was appointed chief of the division of pediatric surgery in the department of surgery at University Hospitals of Cleveland. He also holds the appointment of assistant professor of surgery at Western Reserve University School of Medicine. He assumes the post formerly held by Dr. Edward Gerrish who has entered private practice in Minnesota. Prior to this appointment, Dr. Izant was the associate professor of surgery (pediatrics) at Ohio State University College of Medicine for three years.——Dr. Perry R. Ayres, Columbus, succeeded Dr. Jonathan Forman as editor of the *Ohio State Medical Journal.* Dr. Forman resigned in October. Dr. Ayres was editor and chief of *The Bulletin of the Columbus Academy of Medicine*, having served as associate editor of the publication from 1951 to 1957.

Annual Meeting in Columbus.—The annual meeting of the Ohio State Medical Association will be held April 21-24 in the Veterans Memorial Building, Columbus. The Ohio State Heart Association and the Ohio Division of the American Cancer Society are presenting the first day's programs. Ohio State University College of Medicine will present the final day's program in celebration of its 125th anniversary. Panel discussions to be held at the general sessions include "Treatment of Uterine Cancer," "Cancer of the Gastrointestinal Tract," and "Hypertension," moderated by Dr. Richard L. Meiling, Columbus, Dr. Robert M. Zollinger, Columbus, and Dr. Maurice A. Schnitker, Toledo, respectively. Specialty sections will be conducted April 22-23, including several combined programs. Over 30 guest participants are scheduled to speak, including Dr. Alejandro Aguirre, professor of pediatrics, National University of Mexico, Mexico,

D. F., who will present a paper the afternoon of April 22. Scientific and technical exhibits are planned. The annual banquet, to be held the evening of April 22, will feature the 42 members of the Montgomery County Medical Society Glee Club. For information write the Ohio State Medical Association, 79 E. State St., Columbus 15, Ohio.

PENNSYLVANIA

Philadelphia

Dr. Elliott Heads Hospital Department.—Dr. Frank A. Elliott, of London, arrived in Philadelphia to assume the post of neurologist to Pennsylvania Hospital and head of its department of neurology. This announcement coincided with Dr. Elliott's appointment as professor of clinical neurology, University of Pennsylvania School of Medicine. At Pennsylvania Hospital, Dr. Elliott will establish a neurological center to investigate the causes, treatment, and prevention of the common stroke and related neurological conditions. Funds for this project, amounting to $357,960, have been received as a grant from the John A. Hartford Foundation, Inc., of New York City, established by John A. Hartford, who, prior to his death in 1951, was president of the Great Atlantic and Pacific Tea Co. A native of South Africa, Dr. Elliott received his medical education at the University of Cape Town Medical School.

Open New Laboratory at Hahnemann.—On March 9 Dr. Charles S. Cameron, dean of Hahnemann Medical College, formally opened the 111-year-old institution's third new research laboratory in a year, the Laboratory for the Study of Lipids and Atherosclerosis. The new laboratory, under the direction of Dr. John J. Spitzer, associate professor of physiology, is another step in the planned expansion of Hahnemann's facilities for medical research, following the inauguration of the Institute for Biochemical Studies in Cancer in March, 1958, and the opening of the Cytology Laboratory in February. The Laboratory for the Study of Lipids and Atherosclerosis will chart the distinguishing characteristics between normal and diseased hearts with regard to lipid metabolism and the utilization of energy by the heart. The new facilities occupy an entire floor in a building adjoining the college. Dr. Spitzer has received more than a quarter-million dollars in research funds from the National Heart Institute, and additional support from the Southeastern Pennsylvania Heart Association, and the Smith, Kline, and French Foundation.

City Operates Tuberculosis Institute.—The City of Philadelphia has assumed responsibility for operation of the dispensaries of the Henry Phipps Institute of the University of Pennsylvania, as of March 2, Dr. Julius L. Wilson, director of the institute and professor of preventive medicine at the University, announced March 4. The institute is located at 7th and Lombard streets. Dr. Wilson said this development stemmed from a long period of increasing financial burden on the part of the institute to care for indigent tuberculosis patients. Dr. Wilson pointed out that the city had provided this service on a contractual basis at the Phipps Institute for the past five years. Two other tuberculosis clinics established by the Phipps Institute were long ago transferred to city control. The Henry Phipps Institute was founded in 1903 by the late Henry Phipps for the study, treatment, and prevention of tuberculosis. Present plans include moving its teaching and research activities from the present location to a new building to be constructed adjacent to the planned new West Philadelphia Health Center, which will be located at 43rd Street and Chester Avenue.

GENERAL

Railway Surgeons Meeting in Chicago.—The 71st annual meeting of the American Association of Railway Surgeons will be held April 16-18 at the Drake Hotel, Chicago. At the annual dinner April 17, 7:30 p. m., Dr. A. A. Nygood, Chicago, president of the association, will serve as toastmaster. On April 16, 2 p. m., Dr. David I. Abramson, Chicago, will moderate a symposium on "Peripheral Vascular Diseases," and the afternoon of April 17 Dr. Clifford J. Barborka, Chicago, will moderate a symposium, "Problems in the Management of Peptic Ulcer," as part of a gastroenterology program which includes as a participant Dr. Richard D. McKenna, Montreal, Canada. Surgical and medical movies are planned for the afternoon of April 18. For information write Dr. Chester C. Guy, Secretary, American Association of Railway Surgeons, 5800 Stony Island Ave., Chicago 37.

Orthopedic Meeting in Omaha.—The sixth annual meeting of the Mid-Central States Orthopedic Society will be held April 9-11 at the Town House, Omaha, under the presidency of Dr. Werner P. Jensen, who will open the meeting. Of the papers scheduled, the following will include invited authors:

Tetracycline Fluorescence in Bone Tumors, Dr. John E. McLeay, Omaha.

Experimental Studies and Practical Applications, Dr. Richard E. Ogborn.

Blood Volume Determination, Drs. Lawrence R. James, and L. Thomas Hood, Omaha.

Discussions will follow the papers. A program of tours, a bowling tournament, and other entertainment are arranged, including women's activities. For information write the Mid-Central States Orthopedic Society, 3244 E. Douglas, Wichita 8, Kan.

Anesthesiology Meeting in Birmingham.—The annual meeting of the Southern Society of Anesthesiologists will be held April 23-25 in the Dinkler-Tutwiler Hotel, Birmingham, Ala. Dr. Ralph Berson, dean and vice-president of medical affairs, University of Alabama, Birmingham, will open the meeting with an address. Over 20 papers are scheduled for presentation, and a movie, "Respiratory Resuscitation Techniques," will be shown the afternoon of April 24. A demonstration, "Pump for Extracorporeal Circulation with Possible Demonstration on Patients," will be presented by Drs. Frank A. Berg, Eugene C. Clark, and Champ Lyons, Birmingham. A round-table luncheon is planned for April 23. A program of ladies' entertainment is arranged. For information, write Dr. Ray T. Parmley, 529 N. Hillside St., Wichita 6, Kan., Secretary-Treasurer.

Meeting on Thoracic Surgery.—The 39th annual meeting of the American Association for Thoracic Surgery will be held April 21-23 in Los Angeles with headquarters at the Statler Hilton Hotel. The presidential address will be given April 22, 3 p. m., by Dr. Michael E. De Bakey, Houston, Texas. Forty-two papers are scheduled, including the following by invited participants:

An Improved Inexpensive Automatically Controlled Pump-Oxygenator, Drs. Adrian Kantrowitz, and Donald Abelson, Brooklyn.

An Externally Valved Hydraulic Cardiac Substitute, Drs. I. A. Breckler, R. L. Ginsberg, C. L. Portnoff, and Jack L. Bitterly, Encino, Calif.

A New Foam Plastic Arterial Prosthesis, Richard W. Hardy, Washington, D. C.

The Cause of Death Following Cardioangiography, Dr. Raymond C. Read, Minneapolis, Minn.

The banquet will be held at 7 p. m., April 22. For information write The American Association for Thoracic Surgery, 7730 Carondelet Ave., St. Louis 5, Dr. Hiram T. Langston, Secretary.

World Health Day.—World Health Day, April 7, marks the 11th anniversary of the World Health Organization. In recognition of mental illness as one of the major problems of world health, WHO chose "Mental Illness and Mental Health in the World of Today" as the theme for World Health Day 1959. Dr. M. G. Candau, director-general, World Health Organization, has stated that "in countries with well-developed health services, about half the total number of hospital beds are occupied by psychiatric cases. . . . This increase in mental ill health, involving whole populations, has fortunately been accompanied by rapid progress in the treatment and prevention of mental disease, and also by a better understanding for the psychological strains and stresses that gravely affect everyday behaviour and are not without influence on the well-being of mankind." According to Dr. Candau, World Health Day 1959 offers a suitable starting point in all countries "for a continuing crusade aimed at disseminating better knowledge of mental health problems, ensuring better care for the mentally unfit, and providing better chances for children to grow up in robust mental health."

Arteriosclerosis Society Merges with Heart Association.—The American Society for the Study of Arteriosclerosis merged with the American Heart Association, Dr. Francis L. Chamberlain, president of the association, has announced. The society became the Council on Arteriosclerosis of the American Heart Association. This brings to eight the number of councils now active in the heart association's program. The other councils cover clinical cardiology, cardiovascular surgery, circulation, high blood pressure, rheumatic fever and congenital heart disease, basic science, and community service and education. Since its establishment in 1947 by a group of investigators concerned with this phase of circulatory disease, the arteriosclerosis society has cooperated with the American Heart Association, which was reorganized as a voluntary health agency in 1948. In October, 1958, the society held its annual meeting to coincide with the heart association's annual scientific sessions in San Francisco and several joint programs were conducted. Following an invitation by the association to merge as a council, a large majority of the society's members voted in favor of the amalgamation. The new Council on Arteriosclerosis will hold a scientific session and a symposium as part of the heart association's 32nd annual scientific sessions in Philadelphia, Oct. 23-25, followed by an independent council meeting in November. Officers elected to the new Council on Arteriosclerosis are Dr. James C. Paterson, London, Ontario, Canada, chairman; Forrest E. Kandall, Ph.D., New York, vice-chairman; Dr. Otakar J. Pollak, Dover, Del., secretary; and Dr. Aaron Kellner, New York, program chairman.

Survey of Needs in Tropical Medicine.—The National Academy of Sciences–National Research Council has announced the undertaking of a major survey of needs in tropical medicine. The survey will be directed by Willard H. Wright, Ph.D., recently retired as chief of the Laboratory of Tropical Diseases, National Institutes of Health. Advocated for several years by the American Society of Tropical Medicine and Hygiene, the survey was proposed to the academy-research council by the Department of Defense on recommendation of the Armed Forces Epidemiological Board. Support has now been assured by the National Institutes of Health, the Department of the Army, and the Rockefeller Foundation. The survey will embrace the fields of infectious and parasitic diseases, veterinary medicine, and environmental hygiene. It will include surveys of disease problems in tropical and subtropical areas of significant importance to public health and to agricultural and industrial development; of funds expended for medical care and disease control; of financial support for research in medical and hygienic problems of the tropics; of fellowship opportunities, teaching programs, and training facilities; of career opportunities and incentives; of the impact of travel and migrations on tropical disease problems; of the importance of tropical medicine to the economy of the United States; and of projected manpower needs in terms of domestic and overseas requirements. On the basis of these data it will assess the need for domestic, foreign, and international measures to deal with the problems defined in the survey. The National Academy of Sciences–National Research Council is a private, nonprofit organization of scientists dedicated to the furtherance of science and its use for the general welfare. Its congressional charter, signed in 1863 by President Abraham Lincoln, calls upon the academy to advise the government, upon request, in all matters of scientific and technical interest.

Symposium on Myasthenia Gravis.—The Myasthenia Gravis Second International Symposium in conjunction with the American Academy of Neurology will meet at the Statler–Hilton Hotel, Los Angeles, April 18-19. Papers which include foreign authors are scheduled as follows:

The Neuromuscular Defect in Myasthenia: Electrophysiological and Histopathological Evidence, J. E. Desmedt, Brussels, Belgium.

Some Pathophysiological Mechanisms of Motor Disturbances in Myasthenia, N. I. Grashchenkov and L. B. Perelman, Moscow, U. S. S. R.

Electromyographic Studies in Myasthenia Gravis Correlated to Mechanical Events, Albrecht Struppler and Elizabeth Struppler, Munich, Germany.

A Study of Neuromuscular Transmission in 100 Cases of Myasthenia Gravis, H. C. Churchill–Davidson and A. T. Richardson, London, England.

The Isolation of Quaternary Nitrogen Compounds from Extracts of Thymus Glands, Peter T. Nowell and Andrew Wilson, Liverpool, England.

Some Pharmacologic Properties of Gamma Butyrobetaine, E. A. Hosein, Emma Ottolenghi, and Sheila Dorfman, Montreal, Quebec, Canada.

Recent Work on the Mechanism of Myasthenia Gravis, with Special Reference to the Metabolism of Progesterone, Raymond Greene and I. Schrire, London, England.

The Incidence of Myasthenia Gravis in a Sample Population, George Pennington and Andrew Wilson, Liverpool, England.

Evaluation of Keynes' Large Series of Thymectomies, R. T. Ross, Winnipeg, Canada.

Physiological Concept of the Central Action of the Carotid Sinus, Pierre Passouant, Montpellier, France.

Carotid Sinus Denervation, Andre Thevenard, Paris, France.

A panel, "What Is and What Is Not Myasthenia Gravis?" (Lee M. Eaton Memorial Panel), will be held the morning of April 19, with Dr. Robert B. Aird, San Francisco, as chairman. For information write the Myasthenia Gravis Foundation, Inc., 155 E. 53rd St., New York 10. The program is co-sponsored by the foundation and the National Institute of Neurological Diseases and Blindness.

FOREIGN

Congress on Plastic Surgery in London.—The International Congress of Plastic Surgery, organized by the British Association of Plastic Surgeons, will be held at the Royal College of Surgeons of England, London, July 12-17, under the patronage of His Royal Highness the Duke of Edinburgh. The scientific program will include papers grouped to form symposiums under the following headings:

Surgery of Congenital Deformities
The Surgery of Skin Cancer
Industrial Injuries to the Hand
Trauma of the Face
Cosmetic Surgery
Anesthesia in Plastic Surgery
Research Projects

A Trade Exhibition is being organized at the Royal College of Surgeons. The social program will include the president's reception, a performance at the Royal Opera House, and a banquet on the last night of the congress. For information write Mr. David Matthews, Organizing Secretary, International Congress on Plastic Surgery, c/o Institute of Child Health, Hospital for Sick Children, Great Ormond St., London, W. C. 1, England.

EXAMINATIONS AND LICENSURE

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part II only, April 21-22; Parts I and II, June 16-17; Part I only, Sept. 9-10. Examinations must be received at least six weeks in advance of a specific examination date. Examining centers established after close of registration. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia 4.

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world, Sept. 22. Final date for filing application is June 22. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Written.* Montgomery, June 16-18. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arizona:* *Examination.* Phoenix, Apr. 15-17. *Reciprocity and Endorsement.* Phoenix, April 18. Exec. Sec., Mr. Robert Carpenter, 826 Security Bldg., Phoenix.

Arkansas:* *Examination and Reciprocity.* Little Rock, June 11-12. Sec., Dr. Joe Verser, Harrisburg.

California: *Written.* San Francisco, June 15-18; Los Angeles, Aug. 17-20; Sacramento, October 19-22. *Oral.* San Francisco, June 13; Los Angeles, August 15; San Francisco, November 14. *Oral and Clinical.* San Francisco, June 14; Los Angeles, August 16; San Francisco, Nov. 15. Sec., Dr. Louis E. Jones, Room 536, 1020 N Street, Sacramento.

Delaware: *Examination.* Dover, July 14-16. *Endorsement.* Dover, July 23. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

District of Columbia:* *Written.* Washington, June 8-9. Final date for filing application is May 1. Sec., Dr. Daniel Leo Finucane, 1740 Massachusetts Ave., N. W., Washington.

Florida:* *Examination.* Miami Beach, June 21-23. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Georgia: *Examination and Reciprocity.* Atlanta, June 10-11. Sec., Mr. C. L. Clifton, 224 State Capitol, Atlanta 3.

Guam: *Subiect to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Written.* Honolulu, July 13-14. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination and Endorsement.* Boise, July 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Illinois: *Examination.* Chicago, April 6-9. *Reciprocity.* Chicago, April 10. Supt. of Registration, Mr. Fredric B. Selcke, Capitol Bldg., Springfield.

Indiana: *Examination.* Indianapolis, June 17-19. Exec. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Iowa:* *Examination.* Iowa City, June 15-17. Exec. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines 19.

Kansas:* *Examination and Endorsement.* Kansas City, June. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination.* Louisville, June 8-10. Sec., Dr. Russell E. Teague, 620 South Third St., Louisville 2.

Maryland: *Examination.* Baltimore, June 23-26. Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Michigan:* *Examination.* Ann Arbor and Detroit, June 8-10. Sec., Dr. E. C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave., Lansing 8.

Minneapolis:* *Examination.* Minneapolis, April 21-23. *Reciprocity.* Minneapolis, April 23. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg., St. Paul 2.

Mississippi: *Examination and Reciprocity.* Jackson, June 22-24. Sec., Dr. A. L. Gray, Old Capitol, Jackson 13.

Missouri: *Reciprocity.* Kansas City, April 6. *Examination.* St. Louis, May 29-30. Exec. Sec., Mr. John A. Hailey, Box 4, State Capitol Bldg., Jefferson City.

Montana: *Examination and Reciprocity.* Helena, April 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

Nebraska:* *Examination.* Omaha, June 15-17. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination.* Trenton, June 16-19. Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton 8.

New Mexico:* *Examination and Reciprocity.* Sante Fe, May 18-19. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* New York, Rochester, Syracuse, Buffalo and Albany, June 23-26. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

North Carolina: *Endorsement.* Asheville, May 4. *Written. Examination and Endorsement.* Raleigh, June 15-18. Sec., Dr. Joseph J. Combs, 716 Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, July 8-11. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Ohio: *Endorsement.* Columbus, April 7. *Examination.* Columbus, June 18-20. Sec., Dr. H. M. Platter, 21 West Broad St., Columbus 15.

Oklahoma:* *Examination.* Oklahoma City, June 2-3. Exec. Sec., Mrs. E. L. Haidek, 813 Braniff Bldg., Oklahoma City.

Oregon:* *Written.* Portland, Apr. 17-19. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination and Endorsement.* Philadelphia and Pittsburgh, July 1-3. Sec., Mrs. Margaret G. Steiner, Box 911 Harrisburg.

Rhode Island:* *Examination.* Providence, April 2-3. Administrator of Professional Education, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Reciprocity.* Columbia, May 12; *Examination.* Columbia, June 23-24. Sec., Dr. H. E. Jervey, Jr., 1829 Blanding St., Columbia.

South Dakota:* *Examination.* Sioux Falls, Aug. 25-26. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Texas:* *Examination and Reciprocity.* Fort Worth, June 22-24. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination and Reciprocity.* Salt Lake City, July 810. Dir., Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Virginia: *Examination.* Richmond, June 18-20. *Endorsement.* Richmond, June 17. Address: Board of Medical Examiners, 631 First St., S. W., Roanoke.

Washington:* *Examination.* Seattle, July 13-15. Administrator, Mr. Thomas A. Carter, Capitol Bldg., Olympia.

West Virginia: *Reciprocity and Endorsement.* Charleston, April 13. *Examination.* Charleston, June. Sec., Dr. Newman H. Syer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Written.* Milwaukee, July 14-16. *Reciprocity.* Madison, April 17 and Milwaukee, July 15. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, June 1. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Arkansas: *Examination.* Little Rock, May 4-5. Sec., Dr. S. C. Dellinger, University of Arkansas, Fayetteville.

Colorado: *Examination.* Denver, May 6-7. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Connecticut: *Examination.* New Haven, June 6. Exec. Asst. Mrs. Regina G. Brown, 258 Bradley St., New Haven 10.

District of Columbia: *Examination.* Washington, May 18-19. Address: Mr. Paul Foley, Deputy Director, 1740 Massachusetts Ave., N. W., Washington.

Florida: *Examination.* Miami, June 6. Sec., Mr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Iowa: *Examination.* Des Moines, April 14. Sec., Dr. Elmer W. Hertel, Wartburg College, Waverly.

Kansas: *Examination.* Kansas City, June 2-3. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, May 8-9. Sec., Mrs. Anne Baker, West Michigan Ave., 116 Stevens T. Mason Bldg., Lansing.

Minnesota: *Examination.* Minneapolis, April 7-8. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis.

Nebraska: *Examination.* Omaha, May 5-6. Director, Mr. R. K. Kirkman, Bureau of Examining Boards, 1009 State Capitol Bldg., Lincoln.

New Mexico: *Examination.* Santa Fe, April 19. Sec., Mrs. Marguerite Cantrell, P. O. Box 1522, Santa Fe.

South Dakota: *Examination.* Vermillion, June 5-6. Sec., Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Texas: *Examination.* Austin, Galveston, Houston, Apr. 17-18. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Washington: *Examination.* Seattle, July 8-9. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin: *Examination.* Madison, April 4. Final date for filing application was March 27. Milwaukee, June 6. Final date for final application is May 29. Sec., Mr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

DEATHS

Ansanelli, Francis Cornelius, New York City; Georgetown University School of Medicine, Washington, D. C., 1932; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology; veteran of World War II; associated with the New York Eye and Ear Infirmary, Bronx Eye and Ear Infirmary, and the Lenox Hill Hospital; consulting neurologist for the U. S. Public Health Service; died in the Neurological Institute Dec. 5, aged 53.

Bellamy, Robert Hartlee Ⓜ Wilmington, N. C.; Jefferson Medical College of Philadelphia, 1902; died Dec. 23, aged 77.

Berry, Thomas M. Ⓜ Eldorado, Okla.; Kentucky School of Medicine, Louisville, 1898; served as health officer of Okmulgee County; at one time superintendent of the Western Oklahoma Hospital in Supply; died Dec. 19, aged 84.

Cummins, John Biglow Ⓜ Fort Worth, Texas; University of Nashville (Tenn.) Medical Department, 1897; member of the American Academy of General Practice; in 1950 honored as "Doctor of the Year" in Tarrant County; member of the honorary staff of the Harris Hospital; died Dec. 31, aged 100.

Edwards, Thomas Burton, Cedar Hill, Mo.; St. Louis College of Physicians and Surgeons, 1909; died in St. Joseph Hospital, Kirkwood, Dec. 7, aged 84.

Evans, Albert Lee, Bonne Terre, Mo.; Barnes Medical College, St. Louis, 1900; veteran of World War I; on the staff of the Bonne Terre Hospital; died Dec. 29, aged 87.

Feldman, Joel William, Polk, Pa.; Columbia University College of Physicians and Surgeons, New York City, 1908; staff physician at the Polk State School; died Jan. 20, aged 73.

Ferguson, Allan Harvey Ⓜ Chicago; the Hahnemann Medical College and Hospital, Chicago, 1913; veteran of World War I; associated with the Illinois Masonic Hospital, where he was past-president of the medical staff; died in the Veterans Administration Research Hospital Jan. 19, aged 74.

Freyermuth, Otto George Ⓜ San Francisco; the Hahnemann Medical College and Hospital, Chicago, 1903; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; associated with the Hahnemann and Polyclinic hospitals; psychiatrist for the Criminal Courts in the San Francisco area; died Jan. 19, aged 82.

Gailey, Watson Ⓜ Bloomington, Ill.; born in Ashland, Sept. 7, 1882; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; served on the faculty of the Illinois State Normal University; specialist certified by the American Board of Ophthalmology; past-president of the Central Illinois Society of Ophthalmology and Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; in 1955 vice-chairman, Section on Ophthalmology, American Medical Association; veteran of World War I; medical consultant in India and Guatemala; founder and chief ophthalmologist at the Gailey Eye Clinic; on the staff of the Mennonite Hospital, where he was chief ophthalmologist, and where he died Jan. 19, aged 76.

Gately, George Lynde Ⓜ Revere, Mass.; Tufts College Medical School, Boston, 1918; formerly health commissioner of Boston; member of the American Academy of General Practice; served on the staffs of the Chelsea (Mass.) Memorial Hospital, Winthrop (Mass.) Community Hospital, and the Massachusetts General Hospital in Boston; died Jan. 7, aged 64.

Gentry, Jasper Leonard, Ava, Mo.; Memphis (Tenn.) Hospital Medical College, 1894; Barnes Medical College, St. Louis, 1899; died Dec. 27, aged 85.

Gerding, William John, Newport, Ky.; Medical College of Ohio, Cincinnati, 1897; also a graduate in pharmacy; associated with St. Elizabeth's Hospital, where he was past-president of the staff and where he died Jan. 22, aged 85.

Glover, Mervin Wilbur Ⓜ Arlington, Va.; George Washington University School of Medicine, Washington, D. C., 1932; interned at the George Washington University Hospital in Washington, D. C.; veteran of World War II; died Jan. 9, aged 51.

Griffeth, Frank William Ⓜ Elgin, Ill.; Chicago College of Medicine and Surgery, 1907; member of the staffs of the Sherman Hospital and St. Joseph Hospital, where he died Jan. 19, aged 78.

Haire, Robert Donnell Jr. Ⓜ Glendale, Calif.; Jefferson Medical College of Philadelphia, 1928; formerly associated with the U. S. Public Health Service;

Ⓜ Indicates Member of the American Medical Association.

veteran of World War II; on the staff of the Glendale Sanitarium and Hospital and the Memorial Hospital of Glendale; died Jan. 12, aged 54.

Hale, Joseph Grant, Big Clifty, Ky.; University of Louisville (Ky.) Medical Department, 1907; died in the Grayson County War Memorial Hospital in Leitchfield Nov. 24, aged 78.

Hammill, Hamilton Joseph, New York City; Georgetown University School of Medicine, Washington, D. C., 1931; associated with Fordham Hospital and the Union Hospital, where he died Jan. 21, aged 54.

Harris, John Aaron Ⓜ Webb, Miss.; University of Nashville (Tenn.) Medical Department, 1904; veteran of the Spanish-American War and World War I; died in Jackson Jan. 13, aged 85.

Harryman, William Klipstein Sr. Ⓜ Hackensack, N. J.; University of Virginia Department of Medicine, Charlottesville, 1919; fellow of the American College of Surgeons; veteran of World War I; on the staff of the Hackensack Hospital; died Jan. 13, aged 63.

Harwell, Robert Foster, Los Angeles; Meharry Medical College, Nashville, Tenn., 1936; died Jan. 5, aged 49.

Hawk, Alpha Fritz, Micco, Fla.; Ohio State University College of Homeopathic Medicine, Columbus, 1919; veteran of World Wars I and II; at one time practiced in Urbana, Ill., and served as president of the Champaign County Medical Society; formerly associated with the Veterans Administration Hospital in Jacksonville; died Dec. 16, aged 62.

Helff, Joseph Reuben Ⓜ Keene, N. H.; Jefferson Medical College of Philadelphia, 1914; served on the staff of the Holy Name Hospital in Teaneck, N. J.; died Jan. 8, aged 67.

Hendershot, Otto M., Columbus, Ohio; Baltimore Medical College, 1902; died Jan. 14, aged 90.

Henderson, John M., Williamsburg, Va.; Medical College of Virginia, Richmond, 1895; died Dec. 19, aged 90.

Henricke, Samuel George, Portland, Ore.; Long Island College Hospital, Brooklyn, 1920; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past-president of the North Pacific Pediatric Society; served as president of the medical staffs at Providence Hospital and Portland Sanitarium and Hospital; associated with Holladay Park and Emanuel hospitals; died Jan. 14, aged 62.

Hicks, Oliver Burdette Ⓜ Henderson, Texas; Atlanta College of Physicians and Surgeons, 1907; veteran of World War I; on the staff of the Henderson Memorial Hospital, where he died Jan. 9, aged 79.

Higdon, Edward Franklin, Lincoln, Neb.; University Medical College of Kansas City, 1899; veteran of World War I; served on the staffs of the Veterans Administration hospitals in Virginia and Wadsworth, Kan.; died Dec. 28, aged 83.

Higgins, John Henry Ⓜ Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1903; on the staff of the Asbury Hospital; died Dec. 31, aged 79.

Hill, William Edward, St. Louis; Meharry Medical College, Nashville, Tenn., 1920; a staff member of the Peoples Hospital; died Nov. 29, aged 63.

Hirshfield, Frank R. Ⓜ Minneapolis; University of Minnesota Medical School, Minneapolis, 1921; associated with Doctors Memorial and St. Mary's hospitals; medical director of the Mutual Service Insurance Company; died in the Doctors Memorial Hospital Dec. 16, aged 64.

Hix, Nicholas F. Ⓜ Wise, Va.; University of Virginia Department of Medicine, Charlottesville, 1900; county coroner for many years; died in Bluefield Jan. 1, aged 82.

Hopkins, James Columbus, Hopkinsville, Ky.; Meharry Medical College, Nashville, Tenn., 1917; died Jan. 19, aged 72.

Hosp, Paul Herman Ⓜ Sparta, N. J.; Long Island College Hospital, Brooklyn, 1913; emeritus staff member of Presbyterian Hospital and Martland Medical Center in Newark, where he served on the staffs of St. Michael's and the Babies Hospital–Coit Memorial; died Jan. 20, aged 71.

Hostetter, Robert D. Ⓜ Dayton, Ohio; Jefferson Medical College of Philadelphia, 1916; fellow of the American Academy of Pediatrics; veteran of World War I; on the staff of the Barney Convalescent Hospital; member and once chief of staff at the Miami Valley Hospital, where he died Jan. 12, aged 64.

Hubbard, Isaac George Ⓜ Manson, Wash.; St. Louis University School of Medicine, 1907; died in Chelan Jan. 3, aged 80.

Huff, John Harison, Cosby, Tenn. (licensed in Tennessee in 1903); veteran of World War I; once was a member of the school board; died in Newport Jan. 1, aged 84.

Hughes, Robert Lee Ⓜ Bartow, Fla.; Atlanta Medical College, 1892; past-president of the Polk County Medical Society; formerly practiced in Anniston, Ala., where he was health officer of Calhoun County; served as a member of the state board of health; president emeritus of Bartow Federal Savings & Loan Association; honorary chairman of the board of directors of Citrus and Chemical Bank of Bartow; a charter member and past-vice-president of the Kiwanis Club; honorary staff member of the Bartow Memorial Hospital; died Jan. 6, aged 88.

Hutchins, Clarence Lisle Ⓜ Delta, Ohio; Toledo Medical College, 1908; fellow of the American College of Surgeons; formerly county health commissioner; on the staff of the Detwiler Memorial Hospital; president of the Peoples Savings Bank Company; died in the Toledo (Ohio) Hospital Jan. 11, aged 73.

Jack, Myrtle M., Titusville, Pa.; University of Pittsburgh School of Medicine, 1910; died Dec. 28, aged 84.

Jackson, Fred Douglas, Anniston, Ala.; Meharry Medical College, Nashville, Tenn., 1914; on the staff of the Anniston Memorial Hospital; died Jan. 7, aged 69.

Jameson, Jane Ⓜ Castro Valley, Calif.; University of Wisconsin Medical School, Madison, 1948; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists; served on the staff of the Eden Hospital; died Jan. 20, aged 35.

Jennings, James Francis, Chrisman, Ill.; Starling Medical College, Columbus, Ohio, 1894; served in France during World War I; died in the Paris (Ill.) Hospital Jan. 17, aged 88.

Johnston, James Harvey, San Francisco; Medical Department of the University of California, San Francisco, 1907; died Jan. 2, aged 89.

Jones, Laurence Ⓜ Beverly Hills, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1919; formerly practiced in Kansas City, Mo., where he was associated with the Menorah Hospital; author of "The Postural Complex: Observations as to Cause, Diagnosis and Treatment"; affiliated with Midway Hospital and the Cedars of Lebanon Hospital in Los Angeles, where he died Jan. 5, aged 63.

Jones, Thomas Jefferson, Marion, Ala.; Birmingham Medical College, 1915; served as state senator; died in Selma Jan. 5, aged 72.

Kahle, I. Dana Ⓜ Knox, Pa.; College of Physicians and Surgeons, Baltimore, 1905; served as state representative and state senator; company surgeon for the Baltimore and Ohio Railroad; on the staff of the Oil City (Pa.) Hospital, where he died Jan. 1, aged 83.

Kanter, Aaron Jack Ⓜ Cincinnati; University of Cincinnati College of Medicine, 1934; member of the American College of Chest Physicians; associated with the Jewish and Veterans Administration hospitals; died Jan. 12, aged 49.

Kaufman, Cloid E. Ⓜ Tyrone, N. M.; Chicago Homeopathic Medical College, 1903; died in Silver City Jan. 14, aged 79.

Keene, Fred Floyd Ⓜ Wessington Springs, S. D.; Sioux City (Iowa) College of Medicine, 1908; past school board member, city councilman, justice of peace, and county health officer; veteran of World War I; died in the Royal C. Johnson Hospital in Sioux Falls Jan. 18, aged 80.

King, Gordon Rogers Ⓜ New York City; Howard University College of Medicine, Washington, D. C., 1937; interned at Freedmen's Hospital in Washington, D. C., where he served a residency; died Jan. 21, aged 50.

Kitchell, William Everett Ⓜ St. Clair, Mo.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1903; died in St. Francis Hospital, Washington, Dec. 20, aged 80.

Knowles, Henry Blaine Ⓜ Anna, Ill.; St. Louis University School of Medicine, 1911; formerly associated with the Peoria (Ill.) State Hospital, Anna (Ill.) State Hospital, Illinois Training School for Boys in St. Charles, and the Dixon (Ill.) State School; died Jan. 24, aged 74.

Landry, Paul Bernard, Port Allen, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1904; West Baton Rouge Parish Coroner; served as mayor of Port Allen, member of the Port Allen Town Council, sheriff of West Baton Rouge, and state representative from that parish; chairman, advisory board, East Louisiana State Hospital in Jackson; associated with the Plaquemine (La.) Sanitarium and Our Lady of the Lake Hospital, where he died Jan. 15, aged 78.

Landsborough, Arnold Muir, Garrettsville, Ohio; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1925; died Dec. 5, aged 61.

Lawler, Frank John, Minneapolis; University of Minnesota College of Medicine and Surgery, Minneapolis, 1912; for many years associated with the Veterans Administration Hospital; died Dec. 4, aged 68.

Lawson, Edward Kirby Sr., Harrisburg, Pa.; Temple University School of Medicine, Philadelphia, 1911; fellow of the American College of Surgeons; past president of the Dauphin County Medical Society; formerly associated with the Harrisburg Polyclinic Hospital; served as physician and surgeon for Dauphin County Prison; died Jan. 8, aged 72.

Leader, George Howard Ⓢ Penn Yan, N. Y.; Kentucky University Medical Department, Louisville, 1906; veteran of World War I; on the staff of the Soldiers and Sailors Memorial Hospital; past-president of the Rotary Club; died Jan. 4, aged 76.

Lee, Norman Leon Ⓢ Philadelphia; Howard University College of Medicine, Washington, D. C., 1932; cited by the government for services to the U. S. Selective Service System; died Jan. 11, aged 55.

L'Esperance, Elise Strang Ⓢ Pelham Manor, N. Y.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1899; for many years associated with the Cornell University Medical College in New York City, where she joined the faculty in 1910; past-president of the American Medical Women's Association; fellow of the New York Academy of Medicine; member of the American Association of Pathologists and Bacteriologists, New York Pathology Society, Harvey Society, and the American Radium Society; she and her sister founded the Strang Cancer Prevention Clinic in memory of their mother; a founder and head of the Kate Depew Strang Cancer Prevention Clinic and for many years on the staff of the New York Infirmary for Women and Children; head of a similar clinic, on the staff, and on the board of managers of the Memorial Center for Cancer and Allied Diseases; served as pathologist at the New York Hospital and the Harlem Hospital in New York City; formerly an associate commander of the Women's Field Army of the American Society for the Control of Cancer; in 1942 was presented with the Clement Cleveland Medal, awarded annually by the New York City Cancer Committee "for outstanding contributions to cancer control work;" received a medal, the 1946 award of the American Women's Association; won the 1951 Lasker Award of the American Public Health Association; consulting editor of the *Journal of the American Medical Women's Association;* died Jan. 21, aged 83.

Litterer, Ammon Buist Ⓢ Coral Gables, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1923; clinical assistant professor of dermatology at the University of Miami School of Medicine; veteran of World War II; specialist certified by the American Board of Dermatology and Syphilology; member of the American Academy of Dermatology and Syphilology; associated with St. Francis Hospital in Miami Beach and the Jackson Memorial and Victoria hospitals in Miami; died Jan. 1, aged 61.

Lord, Morris Sheldon, Schenectady, N. Y.; Syracuse University College of Medicine, 1890; veteran of the Spanish-American War; on the honorary staff of the Ellis Hospital, where he died Dec. 30, aged 91.

McConnaughy, James Barth Ⓢ New Kensington, Pa.; University of Pittsburgh School of Medicine, 1918; veteran of World War I; member of the Industrial Medical Association; medical director since 1922 of the New Kensington Works of Aluminum Company of America; on the staff of the Citizens General Hospital, where he died Jan. 7, aged 65.

McKowen, John Ⓢ Baton Rouge, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1912; veteran of World Wars I and II; fellow of the American College of Surgeons; affiliated with Our Lady of the Lake Hospital and Baton Rouge General Hospital, where he died Jan. 4, aged 69.

Martindale, Elihu Arthur Ⓢ Hillsdale, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1899; died in the Foote Memorial Hospital, Jackson, Jan. 1, aged 88.

Magee, Chester Lea, Carmel, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1899; veteran of World War I; consulting physician for the Southern Pacific Railroad; died Jan. 2, aged 88.

Maglio, Murrill Willis, Lepanto, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1925; veteran of World War I; died in the Veterans Administration Hospital in Kansas City, Mo., Jan. 21, aged 61.

Mason, Robert Macon Ⓢ Murray, Ky.; Vanderbilt University School of Medicine, Nashville, Tenn., 1912; affiliated with the Murray Hospital, formerly the Mason Memorial Hospital, of which he was co-founder; a charter member of the Rotary Club; died in the Murray Hospital Jan. 14, aged 70.

Maxwell, Paul Ⓢ Mount Union, Pa.; Medico-Chirurgical College of Philadelphia, 1916; past-president of the Huntingdon County Medical Society; on the courtesy staff of the J. C. Blair Memorial Hospital at Huntingdon; past-president of the Mount Union Rotary Club; died Jan. 1, aged 65.

Mays, William Clifford Ⓢ Stanaford, W. Va.; University of Louisville (Ky.) Medical Department, 1911; veteran of World War I; physician for the New River Coal Company; died Jan. 11, aged 72.

Mercurio, Pasquale James Ⓢ Brooklyn; Boston University School of Medicine, 1937; veteran of World War II; associated with the Norwegian Hospital and the Shore Road Hospital, where he died Jan. 10, aged 46.

Merrill, William Orville Ⓜ Detroit; University of Michigan Homeopathic Medical School, Ann Arbor, 1909; veteran of World War I; for many years chief of the eye, ear, nose and throat department at Highland Park (Mich.) General Hospital; died in the Harper Hospital Jan. 6, aged 73.

Miller, Irvin, New Rochelle, N. Y.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1939; certified by the National Board of Medical Examiners; specialist certified by the American Board of Obstetrics and Gynecology, fellow of the American College of Surgeons; served on the staffs of the New York Polyclinic Medical School and Hospital and the New York Post-Graduate Medical School, New York City; on the staffs of the Lincoln Hospital in New York City and the New Rochelle Hospital, where he died Jan. 26, aged 44.

Miller, Joseph Samuel, Scarsdale, N. Y.; University of Illinois College of Medicine, Chicago, 1933; interned at the Cook County Hospital in Chicago; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association, American Psychosomatic Society, and the American Psychiatric Association; veteran of World War II; on the staffs of the White Plains (N. Y.) Hospital and the New York Psychoanalytic Institute; died Jan. 16, aged 49.

Moorer, William M. Ⓜ Lodge, S. C.; Medical College of South Carolina, Charleston, 1904; chairman of the school board; served as mayor; died in the Colleton County Hospital, Walterboro, Jan. 5, aged 78.

Morris, Roger Sylvester Jr. Ⓜ Ludington, Mich.; University of Chicago, The School of Medicine, 1940; interned at the Henry Ford Hospital in Detroit, where he served a residency; formerly a resident at the Presbyterian Hospital in Chicago and the University of Chicago Clinics; served as assistant professor of medicine at his alma mater; veteran of World War II; died Dec. 30, aged 47.

Muller, Robert Anthony, New York City; born in Carlsbad, Austria, May 18, 1895; Deutsche Universität Medizinische Fakultät, Prague, Czechoslovakia, 1921; specialist certified by the American Board of Physical Medicine and Rehabilitation; member of the American Rheumatism Association and the American Society of Physical Medicine and Rehabilitation; on the faculty of Columbia University College of Physicians and Surgeons; served as director of physical medicine at St. Barnabas, Columbus, and St. Giles hospitals, and the Presbyterian Home; associated with the Presbyterian Medical Center, Lenox Hill and Mount Sinai hospitals, and the Hospital for Joint Diseases; director of physical medicine at St. Luke's Hospital, where he died Jan. 12, aged 63.

Myers, Jacob Ⓜ Sherman Oaks, Calif.; Rush Medical College, Chicago, 1905; served on the faculty of his alma mater; fellow of the American College of Surgeons; formerly practiced in Chicago, where he was on the staff of the Woodlawn Hospital and connected with the Spalding School for Crippled Children; died Jan. 19, aged 75.

Noyes, Edmund Francis Ⓜ Dixon, Wyo.; University of Denver Medical Department, 1897; died in the Memorial Hospital, Craig, Colo., Dec. 31, aged 90.

O'Brien, Joseph Michael, Pittsburgh; Loyola University School of Medicine, Chicago, 1930; veteran of World War II; associated with the Pittsburgh Hospital; for many years county school physician; died Jan. 9, aged 58.

O'Connell, William Michael Ⓜ Nutley, N. J.; George Washington University School of Medicine, Washington, D. C., 1938; veteran of World War II; associated with the Hudson County General Hospital in Secaucus, Berthold S. Pollak Hospital for Chest Diseases in Jersey City, and St. Mary's Hospital in Hoboken; died in the New York Hospital in New York City Jan. 12, aged 46.

Osgood, Frederick Luke Ⓜ Saxtons River, Vt.; born in 1872; University of Vermont College of Medicine, Burlington, 1894; a member of the state board of mental health, on which he served for the past 35 years; served on the Rockingham Board of School Directors for many years; a justice of the peace of the town of Rockingham for 24 years; on Nov. 14, 1954, the state of Vermont dedicated the "Osgood Building" at the Vermont State Hospital in Waterbury in his honor; representative of Rockingham to the legislature from 1917 to 1923 and senator of Windham County from 1921 to 1929; an honorary member of the medical staff at Rockingham Memorial Hospital in Bellows Falls; since 1939 a director of the Bellows Falls Trust Company; died Jan. 10, aged 86.

Parks, Arthur Arnold, Crafton, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; president of the Crafton Board of Health; served on the staffs of the Southside and Allegheny General hospitals in Pittsburgh; died in Pittsburgh Jan. 3, aged 81.

Peterson, Norman Vern Ⓜ Rye, N. Y.; George Washington University School of Medicine, Washington, D. C., 1922; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; emeritus director of the eye, ear, nose and throat department at the United Hospital in Port Chester; died in Avon Park, Fla., Jan. 15, aged 67.

Prichard, Horace De Witt Ⓜ Wichita Falls, Texas; University of Texas School of Medicine, Galveston, 1917; fellow of the American College of Surgeons; honorary member of the staff, Wichita General Hospital; veteran of World War I; died Jan. 9, aged 69.

Quinn, Raymond James Ⓜ Waterbury, Conn.; College of Physicians and Surgeons, Baltimore, 1913; veteran of World War I; served as city bacteriologist and welfare department physician; associated with St. Mary's Hospital, where he died Jan. 13, aged 66.

Riecker, Herman Harlan, Ann Arbor, Mich.; Johns Hopkins University School of Medicine, Baltimore, 1923; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the American Society of Clinical Investigation; veteran of World War I; past-president of the Washtenaw County Medical Society; for many years on the faculty of the University of Michigan Medical School; on the staff of St. Joseph Mercy Hospital, where he died Jan. 4, aged 63.

Robertson, Jarratt Padgett Ⓜ Birmingham, Ala.; Vanderbilt University College of Medicine, Nashville, Tenn., 1923; specialist certified by the American Board of Urology; member of the American Urological Association and past-president of the Southeastern section; associate professor of urology at the Medical College of Alabama; associated with South Highland Infirmary, Crippled Children's Clinic Hospital, University Hospital, and St. Vincent's Hospital; died in the South Highland Infirmary Jan. 17, aged 60.

Ross, Thomas Trigg Ⓜ Gurdon, Ark.; Tulane University School of Medicine, New Orleans, 1928; health officer of Clark County; specialist certified by the American Board of Preventive Medicine; for many years state health officer; died Jan. 1, aged 60.

Scales, John Perkins Ⓜ Livingston, Ala.; Louisville (Ky.) Medical College, 1897; past-president of the Sumter County Medical Society; veteran of the Spanish-American War and World War I; served as physician to Livingston State College from 1930 to 1946; formerly county health officer; for many years surgeon for the Southern Railway; died in the Veterans Administration Hospital, Tuscaloosa, Dec. 30, aged 87.

Sheldon, Edward Schock, Ewan, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1895; for many years practiced in Collingswood, where he was first health officer and organized the board of health; for many years attending physician at the Methodist Home for Aged in Collingswood; president of the first Collingswood Bank and member of the board of health; one of the founders and formerly on the staff of the West Jersey Hospital in Camden, where he died Dec. 20, aged 84.

Smith, Lester Alvin Ⓜ Indianapolis; Rush Medical College, Chicago, 1916; specialist certified by the American Board of Radiology; member of the American Roentgen Ray Society and Radiological Society of North America; fellow of the American College of Radiology; associate professor of radiology at the Indiana University School of Medicine; veteran of World War I; member of the staffs of Methodist, St. Vincent's, and Indianapolis General hospitals; died Dec. 15, aged 68.

Speicher, George Franklin Ⓜ Somerset, Pa.; Baltimore Medical College, 1910; for many years a member of the school board of Rockwood, where he was a director of the Union National Bank and the Coal Operators Casualty Company; associated with the Somerset Community Hospital and the Somerset State Hospital; died Dec. 25, aged 75.

Stoughton, Arthur Volney Ⓜ Claremont, Calif.; Ohio Medical University, Columbus, 1898; served on the faculty of the Pomona College, where he was college physician; first president of the Pomona College Alumni Association; died Dec. 26, aged 86.

Summers, William Boyd Ⓜ Casper, Wyo.; University of Colorado School of Medicine, Denver, 1951; interned at Mount Sinai Hospital in Miami Beach, Fla.; served a residency at the Veterans Administration Hospital in Denver; on the staff of the Memorial Hospital of Natrona County; died in Denver Dec. 1, aged 32.

Wells, William Albert Jr., Washington, D. C.; Howard University College of Medicine, Washington, 1907; also a graduate in law and pharmacy; served on the faculty of his alma mater; died in Washington Hospital Center Dec. 19, aged 85.

FOREIGN LETTERS

AUSTRIA

Cerebral Lipoidoses.—At the meeting of the Austrian Pediatrics Society in January, Dr. H. F. Seitelberger said that cholesterol thesaurismosis, phosphatide thesaurismosis, amaurotic idiocy, lipochondrodystrophy, and lipid histiocytosis are essentially endogenous cellular enzyme disturbances in the metabolic chains of the sphingolipoids: ganglioside, cerebroside, and sphingomyelin. The blockage of certain enzymatic reactions leads to pathological storage of certain substances within the cells. The storage or accumulation of a certain lipoid in each case is caused by the blockage of a distinct enzymatically regulated reaction within the metabolic chain of the sphingolipoids. In lipochondrodystrophy, the most frequent of this group of diseases, not only is ganglioside stored in the cells of organs, but also the mucopolysaccharide-lipoid complex. The disturbance responsible for this storage is to be found at a connecting point of the lipoid and polysaccharide metabolism. It is characteristic of lipid histiocytosis that cerebroside storage takes place exclusively in the reticulohistiocytic system, that is, in the brain it takes place only in the periadventitia of the vessels. The speaker stated that the anatomic differences between the infantile, late infantile, adolescent, and other forms of amaurotic idiocy are to be found in the degree of penetrance of the existing genetic enzyme disturbance. In the presence of a gene mutation of high penetrance, the disease will begin early and will be severe and short. The postinfantile forms with lesser penetrance are of longer duration, and the lesions in the brain are less severe, have local fluctuations in intensity, and show characteristics pointing to the manifestation of vital cellular reactions to the disease process.

In commenting on this report, Dr. H. H. Gross, of the Neurohistological Laboratory of the Mental Hospital of Vienna, stated that so far studies were made on 546 brains of patients in whom severe imbecility had been diagnosed as either congenital or acquired in early childhood. Contrary to expectation, the percentage of patients with cerebral lipoidoses was small. Only five cases of lipochondrodystrophy and three of amaurotic idiocy were found. He admitted, however, that whereas the clinical diagnosis of lipochondrodystrophy, thanks to its characteristic physical symptoms, causes no difficulties, the recognition of the various forms of amaurotic idiocy is still difficult, particularly if the patient has no history of a familial tendency.

BELGIUM

Lysosomes.—At a meeting of the Medical Academy Dr. De Duve of Louvain stated that lysosomes were first recognized in the liver. They are corpuscles with a diameter slightly smaller than half a micron, and contain an enzyme in a lipoprotein casing. They act only in an acid environment and only after the rupture of the protective casing. They have been detected in the kidney also, where they seem to be indistinguishable from particles recognized by Gerard and Cordier as having the power of phagocytosis. The role of the lysosomes is still unknown but it is believed that they may play a part in autodigestive and degenerative phenomena.

Hiatal Hernia.—At a meeting of the Belgian Society of Gastroenterology a symposium on hiatal hernia was presented. This condition was attributed to such factors as old age, obesity, abdominal hypertension, endocrine disturbances, and pregnancy. Le Cluyse of Brussels reported a series of 36 patients and concluded that the incidence of hiatal hernia could not be accurately determined because many patients are asymptomatic. The associated pain may be due to esophagitis, esophageal reflux, or incarceration of the hernia. Operation is indicated for acute hemorrhage of the upper gastrointestinal tract and constant or recurrent pain. Medical treatment is only palliative. The speaker stressed the diagnostic value of gastroscopy in these patients.

Deloyers and van der Stricht emphasized the necessity of evaluating the surgical treatment of hiatal hernias. Correction of the anatomic defect should relieve symptoms and restore normal functions. The speakers preferred a modification of Allison's technique. Deloyers emphasized the importance of team work by the internist, gastroenterologist, cardiologist, roentgenologist, and surgeon. Recurrences are seen in about 10% of those operated on. This is because of the friability of the tissues of this region.

CHILE

Penicillin and Rheumatic Heart Disease.—An investigation of the effect of penicillin on acute rheumatic fever and valvular heart disease was undertaken in the Jose Joaquin Aguirre and Roberto del Rio hospitals of Santiago, under the sponsorship of the Commission on Streptococcal Diseases, U. S. Armed Forces Epidemiological Board, the Western Reserve University School of Medicine, the University of Chile, and the Chilean National Health Service. The results of the first year of the study were reported by Mortimer and co-workers (*Revista médica de Chile*, vol. 87, 1959). In this series of 97 patients with acute rheumatic fever, 49 received large doses of penicillin for six weeks, and 48 controls received no antibiotic. The penicillin appeared to have no effect on the acute clinical, laboratory; and electrocardiographic manifestations of the disease but did reduce the incidence of valvular heart disease; 52% of the control group exhibited valvular disease one year after the acute attack as compared to only 21% of those who received penicillin. The disparity between the effects on the acute manifestations and those on endocardial lesions suggests two pathogenetically different processes. The observed effects of penicillin indicate that valvular heart disease may depend in part on a continuing stimulus from living streptococci, even after the symptoms of rheumatic fever have disappeared. It is concluded that an intensive course of penicillin is justified as a preventive of valvular heart disease.

Health Progress.—According to the Yearbook of Causes of Deaths of the Department of Vital Statistics, there has been a great progress in the lowering of the death rate in the 10 years, from 1948 to 1957. The crude death rate dropped from 16.9 to 13.7 deaths per 1,000. The infant mortality (deaths under one year of age) decreased from 145.9 to 117.7 deaths per 1,000 live births in the same period. This is still much too high. In the same period the crude birth rate increased from 35.9 to 38.4 births per 1,000 population. A new maternal health law provides payments for mothers from the sixth month of pregnancy on if they accept treatment by the Mother and Child Welfare Department of the National Health Service.

FRANCE

Irradiation and Marrow Transplantation for Leukemia.—Prof. J. Bernard and Dr. G. Mathé, with a team of doctors at the Hospital St. Louis in Paris, treated a 13-year-old girl with acute leukemia by a combination of irradiation and injections of bone marrow from human donors. Although the method had been used experimentally in mice, this was the first human patient to be so treated. The trial was made as a result of the information obtained from the treatment in Paris of six Yugoslav scientists who accidentally received lethal or near-lethal doses of radiation from an experimental atomic reactor. They were saved by human marrow transfusions. These would normally be rejected owing to the formation of antibodies in the host, but irradiation just before the transfusion prevents this process. The girl was irradiated by exposure to 300 r from a cobalt bomb. This served the double function of destroying the leukemia cells and inhibiting the formation of bone marrow antibodies. Four transfusions of bone marrow from healthy donors were then given. The blood count returned to normal within a month. When last seen the girl was continuing to improve.

INDIA

Vitamin Deficiency and Gestoses.—Pai and Pate (*Indian Journal of Medical Research*, vol. 46, September, 1958) studied the relationship between thiamine, riboflavin, and niacin deficiency and the occurrence of toxemia of pregnancy. The excretion of thiamine, riboflavin, and niacin in toxemic patients was studied in 24-hour urine specimens before and after delivery. A test dose of 5 mg. each of thiamine and riboflavin and 50 mg. of niacin was given orally and the excretion of the respective vitamins was estimated. The urine specimens were collected on the 1st, 2nd, 5th, 6th, 10th, and 11th days after delivery and the results compared with those in normal subjects and in normal pregnancy. A deficiency in thiamine was found in the toxemic patients. This decreased after the test dose. The recovery was manifested clinically by the disappearance of edema and albuminuria and a gradual reduction in blood pressure.

The thiamine return after the test dose in patients whose pregnancy was normal was much lower than that in the nonpregnant control group. The dietary intake was 0.7 mg. of thiamine, 0.6 mg. of riboflavin, and 6 mg. of niacin daily, while in those with normal pregnancy these values were 0.85, 0.8, and 7 mg. respectively. There was no correlation between the dietary intake and the urinary excretion of these vitamins in toxemia or normal pregnancy. The percentage return of thiamine after the test dose in toxemias of pregnancy studied on 1st-2nd, 5th-6th, and 10th-11th days was significantly lower than that in the nonpregnant group, thus showing a state of unsaturation with regard to thiamine. Low values for riboflavin were obtained only in the first-second-day period, showing that unsaturation here existed only during this period, while no state of unsaturation was revealed with regard to niacin.

Action of Hormones on Involuntary Muscles.—A. P. Sharma (*Indian Journal of Medical Research*, vol. 46, September, 1958) stated that epinephrine, acetyl choline, and histamine are widely liberated in the body and play a vital role in regulating tissue functions by virtue of their local actions. These actions have been studied mainly on cardiac and involuntary muscles where they produce motor or inhibitory effects which vary in different animals, in different systems, and in the same system at different sites. Dual effects (both stimulation and inhibition of the same tissue) have also been observed. The activity of involuntary muscles is also influenced by the concentration of sodium, potassium, and calcium ions in body fluids. The author therefore studied the mechanism of these local hormones and the role of electrolytes, if any, in this mechanism. Experiments were conducted on the involuntary muscles of the isolated small intestine of rabbits. Epinephrine had an inhibitory effect under aerobic conditions, which was changed to stimulation under anaerobic conditions by previous treatment with acetyl choline, atropine, and potassium chloride. Sodium or calcium chlorides did not affect its action. Acetyl choline produced a stimulation under both aerobic and anaerobic conditions which was changed to inhibition by previous treatment with epinephrine, sodium chloride, and calcium chloride. With potassium chloride, stimulation was produced under both aerobic and anaerobic conditions.

Atropine in all concentrations and under both aerobic and anaerobic conditions inhibited the small intestine after preliminary stimulation. Stimulation was, however, produced after previous treatment with calcium chloride, though the antagonizing action to acetyl choline was retained. The stimulating action of histamine was changed to inhibition by previous treatment with atropine, calcium chloride, or potassium chloride. Sodium and potassium caused stimulation of intestinal activity; after previous treatment with the other electrolyte, stimulation was replaced by inhibition. Acetyl choline changed the inhibitory action of sodium and potassium chloride into stimulation. Epinephrine enhanced the inhibitory action of both. Calcium chloride caused a depressant action which was reversed by previous treatment with atropine. Thus it was seen that the effects of these local hormones and electrolytes varied, depending on the previous state of the intestine, and changed with changes in the electrolyte concentration of the surrounding fluid and also previous treatment with some other hormone. Most of them could produce either stimulation or inhibition. The different actions of these hormones in different sites and different species may be due to the different environmental conditions present at the time. This may possibly explain the different actions of local hormones on the involuntary muscles in different regions.

Urinary Excretory Patterns, Glucose Tolerance, and Shock Therapy.—N. G. Srinivasan and co-workers (*Indian Journal of Medical Research*, vol. 46, September, 1958) studied the urinary excretion of amino acids and the glucose tolerance of catatonic schizophrenic patients before and after electroconvulsive therapy. Urine samples were collected prior to the shock treatments, on days subsequent to the 7th and 10th treatments, and on the 5th and 10th days after termination of shock treatment. A marked fall in the excretion of most of the amino acids after the seventh shock was seen. With subsequent shocks there was a slight tendency for these values to rise but they never came back to the original level. The low values were maintained for some time even after termination of the therapy. Particularly low levels were obtained for glutamic acid, glycine, threonine, and aspartic acid. The glucose tolerance and other biochemical studies were also made prior to the shock treatments, after the 1st, 4th, 7th, and 10th treatments, and on the 4th, 7th, and 10th days after termination of the shock treatment. The total proteins, albumin, and potassium levels showed a significant rise, returning gradually to normal after the last electroconvulsive shock. The two-hour glucose values after shock were higher than the preshock values. The inorganic phosphate levels showed a significant fall corresponding to the levels of glucose, showing their utilization in the metabolism of glucose. Both tended to return to fasting levels after termination of the shock therapy, particularly on the 10th day after this termination.

Vitamin B_{12} and Nitrogen Metabolism.—B. D. Punekar (*Current Medical Practice*, vol. 2, December, 1958) studied the effect of vitamin B_{12} on the digestibility coefficient and nitrogen retention in rats. Male weanling albino rats distributed into two groups according to their body weights were served a corn and soy bean diet adequate in all vitamins except vitamin B_{12}. One group received this vitamin by injection in a daily dose of 0.2 mcg. for four weeks. A higher growth response was noticed in the group receiving vitamin B_{12}, suggesting a specific function for this vitamin in anabolism. These rats gained in weight much more rapidly than those without the vitamin. The digestibility coefficient did not show any significant difference in the two groups but a marked difference was seen in the amount of nitrogen retained in the presence of vitamin B_{12}, a much higher retention of nitrogen being noticed with its administration.

Meeting of Public Health Association.—At the third annual meeting of the Indian Public Health Association in Calcutta in December, Dr. Das Gupta criticized the meager expenditure on health under the First Plan. The problem of nonavailability of trained personnel could be solved if language or customs were not considered insuperable barriers to employment and service. Although scientific investigation for better control of tuberculosis is being made, scant attention has been paid to rehabilitating patients cured of tuberculosis. The control of leprosy, cholera, and smallpox must be undertaken on a national scale. Referring to such virus diseases as poliomyelitis and encephalitis, he said that each State Directorate should have a trained epidemiologist. There should be a central laboratory in each state provided with a virology unit. A midday meal should be provided for children in schools. More attention should be given to mental disorders. Finally, a medical section must be attached to each factory for the care of the workers.

Rupture of the Uterus.—N. S. Devi (*Current Medical Practice*, vol. 2, December, 1958) observed 41 cases of uterine rupture in 17,882 deliveries. This high incidence was due to inadequate facilities for antenatal care, most of these accidents occurring in the patients' homes, the distance between the home and the hospital in some cases being 75 miles. Only one patient in the series had had antenatal attention. Most patients were under 30 years of age, the youngest being 16 and the oldest 35. There was only one primigravida in this series, the parity varying between two and nine. Of the multiparous women in this series six had an otherwise normal labor when the accident occurred. Dystocia accounted for 18 of the cases. The labor was not prolonged in all these cases, its duration varying from 2 to 48 hours. Preexisting scars in the uterus accounted for nine cases. Three were due to excessive penetration by chorionic elements. There were five cases of traumatic deliveries in which internal podalic version was performed; the labor was prolonged and there was excessive retraction of the uterus over the fetus. Six multiparas had a normal vertex presentation and the rupture was at the cervicovaginal junction. Previous labors had been uneventful. The site of rupture was the lower uterine segment in 19 patients, the upper uterine segment in 9, the broad ligament in 7, and there was colporrhexis in 6. There were 18 maternal deaths (44% mortality) and 38 fetal deaths (92.7% mortality). Eight died before treatment could be given, 1 was given conservative treatment because she was unfit for surgery, and 32 were given total or subtotal hysterectomy.

Hypothermia in Cardiovascular Surgery.—Padhi and Nanson (*Journal of the Indian Medical Association*, vol. 31, Dec. 1, 1958) performed cardiovascular operations on 10 patients under hypothermia; 7 of these had atrial septal defect with marked shunts, 8.3 to 13.1 liters per minute passing through the defect, mainly left to right; 1 had a pulmonic stenosis and was operated on under direct vision; and 2 had aortic insufficiency of rheumatic origin. Here hypothermia was used as an adjunct, and was thought to give an added margin of safety. These two patients were cooled to 32 C and the aorta was clamped for 12 and 7 minutes respectively. For the patients with auricular septal defects, the time of circulatory interruption varied from 2.5 to 10 minutes and for the patient with pulmonary stenosis, the circulation was interrupted for 2.5 minutes. The rectal temperature during circulatory interruption varied from 28 to 32 C (82.4 to 89.6 F). All patients recovered.

NEW ZEALAND

Fee-for-Service Scheme for Medical Care.—The supplement to the *British Medical Journal* of Feb. 14 contains an article by A. W. S. Thompson, director of the division of clinical services, Department of Health, New Zealand. He discussed the existing (since 1941) fee-for-service scheme, and proposed modifications which should do away with the existing scheme's disadvantages. In New Zealand the government pays a benefit of up to $1.05 for each service by a general practitioner, increased to $1.75 for night, Sunday, or holiday services. Specialist services qualify for the same benefit, but, whereas the general practitioner can claim an extra fee from the fund for prolonged attendance (over 30 minutes), the specialist cannot. The benefit is intended to help the patient to pay the physician's bill. The physician is free to charge what he likes, within reason, the standard charge in general practice, over and above the benefit, being 70 cents for an office visit and $1.05 for a house call. Some doctors still accept the benefit as full payment. The benefit has remained unchanged since 1941.

The fee-for-service scheme works in two ways. Under the refund system the doctor sends out bills in the ordinary way, and patients obtain refunds on the basis of their receipted accounts. This method involves practically no government intervention in ordinary practice. About 25% of doctors, most of them specialists, work on this system. The alternative is the schedule system. The doctor takes only his extra charges (if any) from the patient direct, and claims the benefit by submitting to the Health Department daily schedules listing all patients attended. Most doctors send in their schedules fortnightly or monthly. No patients' signatures are required, but 1% of claims are checked by postal inquiry. The advantages of fee-for-service on these lines over any type of capitation scheme are that there is no contract of service between the private practitioner and any member of the public (the physician is not "bound to his patient by the iron fetters of a legal contract enforceable day and night at the whim of the patient") and that there is free choice on both sides. The result is that complaints about failure to attend patients, or of rudeness or arrogance on either side over calls at inconvenient times, while not unknown in New Zealand, are much rarer than they appear to be in Great Britain, and have no legal significance.

The refund method is excellent but has two defects from the medical point of view. One is that no benefit is payable unless the patient first settles the doctor's bill, and in consequence all refund practitioners have a proportion of bad debts. Even if the doctor charges no more than the bare amount of the benefit, some patients fail to pay their bills. For this reason there has been a tendency in recent years for doctors to change from refund to schedule. A similar but more serious defect is that it would be a hardship for many patients to have to find the cash to pay their accounts in full, even though they could afterward obtain refunds for all or most of the amounts due. Some practices could hardly be run on a refund system, despite full employment and a high living standard. Both public and doctor would suffer if such a system were universal.

A simple modification of the fee-for-service scheme that would correct most of its faults is the patient schedule system. Doctors would be paid so much by the state for every patient seen in any calendar month, irrespective of the number of times the patient had been seen in that month. In all other respects the scheme would be worked exactly as the fee-for-service schedule system works now. There would be no interference with the refund system, which has no serious defects so long as it is not compulsory. A global sum is agreed on to represent 67% of the agreed aggregate gross income of all general practitioners. For the first few years of the new scheme 8.3% of this pool would represent the sum to be distributed monthly. Doctors would submit a certified return of patients seen, giving date of first attendance in that month only. After about five years it should be possible to arrive at an agreed amount to be paid per patient per month, and the pool system could then be abandoned.

UNITED KINGDOM

Goiters in School Children.—A survey of school children in North Oxfordshire showed a relatively high incidence of thyroid enlargement. The mean incidence of enlargement was 40%, compared with 6% in Oxford city. The normal limit for adolescents is about 3%. A survey made 15 years ago showed that an increase in thyroid enlargement of 27% has occurred since then. The district in question lies on a belt of limestone and marl (clay mixed with calcium carbonate) soil that is deficient in iodine. Water drawn from local wells contained from 0.6 to 3.9 mcg. of iodine per liter. Levels below 3 mcg. are considered to be goitrogenic. Owing to its high calcium content the water is hard, and such water is thought to interfere with the utilization of iodine. Most of the milk and farm produce in this goitrogenic area is grown locally, in iodine-deficient soil, whereas the food eaten in Oxford city is obtained from national markets.

Smoking in Schools.—A survey of the smoking habits of 8,314 children in Oxfordshire schools by a health officer revealed that 193 boys were aged 7 or less when they smoked their first cigarette. Of 4,270 boys interviewed, 2,853 or 67% had tried smoking, and 1,245 or nearly 30% had continued to do so. Of 4,044 girls interrogated, 1,276 or 31.5% had tried smoking, but only 328 or 8% had continued the habit. Family influence played a part in determining whether the children smoked or not. Less than 20% of those who smoked came from families where the parents did not smoke. When both parents smoked the chances that their children would smoke were three times as great as in nonsmoking households. The places where the children smoked were mainly in the home and at the cinema. One of the girls smoked 75 cigarettes a week.

Cutaneous Leishmaniasis.—At a meeting of the Royal Society of Tropical Medicine and Hygiene Prof. P. Garnham and Dr. D. Lewis referred to the rising incidence of cutaneous leishmaniasis in collectors of chicle in British Honduras. These workers enter the forests at the beginning of the rainy season, live a nomadic life moving from one camp to another, and go back to their families when the rainy season is over. Their lesions are found mainly on the ears. The ulcers are chronic and ultimately lead to destruction of the organ involved. An animal reservoir for the causative parasite appears probable, as the chicle gatherers are so sparsely distributed and stop such a short time in one spot that the usual vector, the Phlebotomus, would have little opportunity or time to acquire the infection from one person and pass it on to another. Fourteen species of Phlebotomus were found on local animals. The most satisfactory control measure would probably be an attenuated vaccine.

Emotional State and Energy Expenditure.—It has been generally supposed that euthyroid nervous subjects show a tendency toward a high basal metabolic rate and that diagnostic errors due to emotional upsets may easily be made. This view is challenged by Melville and Mezey (*Lancet* 1:273, 1959), who investigated the strength of the association between the emotional state and oxygen requirements in the lying, sitting, and standing positions in 32 psychiatric patients and 10 healthy subjects. The serum protein-bound iodine levels of all subjects were within the normal range. The psychological state, which varied from almost normal to severe delusional fear, was estimated on a four-point system referring to symptoms indicating emotional disturbance. Two independent ratings were made, one before testing and the other during the test procedure. It was expected that the more disturbed patients would show higher energy expenditures than the controls, but the results did not confirm this. The mean oxygen consumption of the mentally disturbed patients was not significantly different from that of normal subjects in the lying and sitting positions, and was actually less in the standing position. The most striking finding was the absence of any relationship between emotional state and rate of oxygen consumption.

Sterilizable Blankets.—Woolen blankets are a potent source of cross-infections in hospitals because they attract bacteria and disseminate them in lint. Attempts to sterilize blankets reduce their life to a matter of months. Calnan (*Lancet* 1:300, 1959) solved the problem of the hospital blanket after studying the method used by the Everest expedition for keeping warm. The mountaineers wore string vests under a wind-proof garment. The blanket substitute, which resembles a string vest in structure, consists of a warp-knit mesh fabric of viscose and cotton between two cotton sheets. The three layers are quilted together on a sewing machine. Cotton sheeting is attached to each side of the blanket substitute to allow for a tuck-in. Such blankets have been in use for over a year. After their introduction there was a noticeable reduction in the amount of dust and lint in the wards. The blankets, unlike woolen ones, can be sterilized by boiling or autoclaving without loss of texture.

Health and Social Class.—At a meeting of the British Sociological Association in January Dr. J. N. Morris said that preventable disease is more likely to occur in those of lower social class, because it takes longer for the less educated sections of the population to benefit from the newer knowledge on child rearing, advances in medical science, and medical services offered by the state. On the other hand, social class is not as rigid as it was formerly. There is now greater mobility up and down the social scale, which is largely based on income, status, and residence. It appears that the mentally and physically healthy move up and the unfit move down the social ladder. There has always been, and still is, a substantially higher death rate among the economically underprivileged. There is a closing of the social classes with respect to illness in children. Mortality and morbidity are decreasing more rapidly in children of the lower social classes. A study of the death rate from rheumatic heart disease or the incidence of chronic otitis media shows this.

Dr. Morris drew attention to the preponderance of schizophrenia among the unskilled young men of the lowest social class, which is a result of the mentally unbalanced dropping into a lower income group on account of their illness and lack of earning capacity. Poliomyelitis, on the other hand, is a relatively new disease affecting chiefly those of higher social classes. There is an inverse relationship of paralytic poliomyelitis to the level of sanitation and to infant mortality. Lung cancer and duodenal ulcer, which showed no relation to social class 20 years ago, now show a rising mortality with a fall in the social scale from higher to lower class. Coronary artery disease, which has an increased incidence in higher social classes, appears to be associated with limitation of physical activity. This is understandable, as a rise in social class is associated with a more sedentary job and diminished physical activity. Light workers 45 to 54 years of age show the same rates of ischemic myocardial fibrosis in all the social grades. A rise in the standard of living, with its decrease in physical work, is likely to increase the incidence of coronary artery disease.

Smog.—In the last week of January smog in Britain, particularly in the northwest, was stated to be the worst in living memory. The demand for hospital beds increased sharply owing to the smog aggravating chronic respiratory ailments, especially among the elderly. In Salford the smog appeared as a widespread smoky haze limiting visibility to 200 yd. or less. In this town the smoke averaged 120 mg. per 100 cu. m. and the sulfur dioxide 0.35 ppm. At one period the smoke figure rose to 478 mg. per cubic meter and the sulfur dioxide to 1.64 ppm, about eight times the January average. The demand for hospital beds was so great that hospitals rejected applicants unless their need was urgent. In 1956 the Clean Air Act was passed. Attempts are being made to implement this by creating smokeless zones and by discouraging the use of open coal fires in homes. In the last two years more than 125 local authorities in England and Wales decided to use their powers under the act to enact smoke-control orders. Unfortunately, the "black areas," where smog is most frequent and morbidity from respiratory disease is highest, are among the slowest to comply with the orders.

Influenza.—Influenza has reached a peak in London, whose inhabitants are also suffering from colds, bronchitis, and other respiratory diseases. These are undoubtedly associated with winter fogs and atmospheric pollution. There is a great demand for hospital beds and the services of general practitioners. The London Local Medical Committee, which represents 2,000 doctors in the London area, sent out a request to 3,250,000 patients to defer calling in the physician unless it is absolutely necessary. Patients have also been asked to make their telephone calls early in the day so that the physician can arrange his visits accordingly. In many districts physicians are finding it difficult to cope with the additional sickness. Patients are asked to defer visits for a week or two if their condition does not need immediate treatment. Hospitals have been told to restrict admissions to emergency cases only. The influenza epidemic is mild. Very few deaths have been reported. Although some of the attacks are attributed to the Asian virus, most of them are probably due to virus B. School children are suffering most. Many schools are only half-filled because of influenza, measles, chickenpox, and bad colds. In one area scholarship examinations of 11-year-old children have been deferred because of absence. In Blackpool there is much absenteeism due to "four day influenza." At Ripley Hospital in Derbyshire no more operations are being performed for the time being because of influenza among the patients and staff.

Militarized Medicine.—Sir George Schuster, chairman of the Oxford Regional Hospital Board, in a survey made for the Acton Society Trust suggested that the Ministry of Health be reorganized and remodeled along army lines (Creative Leadership in a State Service, London, 1959). He considered that the hospitals should be regarded as part of a fighting service and that heads of hospital boards should look to the Ministry of Health for leadership and direction in the same way that army commanders do to their commander-in-chief. Medicine would then have two top posts corresponding to the chief of the imperial general staff and to a combination of the posts of adjutant general and quartermaster general. These positions would be occupied by persons with hospital experience at an operational level. A new type of skilled administrator is needed in the health service, according to Sir George. At present there are not enough top management posts in the hospital service and the pay for those that do exist is inadequate.

Sir George criticizes the present scheme of hospital management. At present this is largely autonomous and in the hands of boards and committees whose members are mainly unpaid volunteers from the hospital staff. They are entrusted with the spending of large sums of money. While he admits the value of such voluntary effort, he believes that economy and efficiency would be improved by intensive, expert study of hospital costs and by the use of work-study programs and other efficiency techniques. While it would be inadvisable to replace this volunteer system entirely by paid officials, it is thought that efficiency would be improved by the introduction of professional administrators, and the formation of central intelligence and statistical departments.

Unlawful Attendance at Wife's Confinement.—A man pleaded guilty to attending his wife's confinement without medical supervision and not in an emergency. This is an offense under the Midwives Act, which requires that only a midwife or doctor may attend a confinement except in emergencies when they are not available. A woman consulted her physician early in her pregnancy and informed him that she would like her husband present when the baby was born. As the physician disapproved she decided to do without him. The pregnancy and puerperium were normal and uneventful. The prosecution was brought by the local county council, which sent a health visitor to see the baby after the husband had sought advice about obtaining a maternity allowance under the National Health Service. The judges gave her husband, who pleaded that he did not know that he was committing an offense, a conditional discharge.

Reduction of Carcinogens in Tobacco.—Dr. E. Wynder (*British Medical Journal,* Feb. 7, 1959) stated that man will continue to smoke, whatever evidence is presented regarding an association between tobacco and cancer. The most practical solution is to render tobacco smoke noncarcinogenic, or at least to reduce its carcinogenicity. This can be done by lowering the tar content of tobacco, reducing the temperature of combustion, and modifying its pyrolysis. It is unlikely that the tar content of tobacco can be reduced by any great extent by effective selection, as the various kinds of tobacco have much the same carcinogenic activity; but an effective filter would help. This practical step should be undertaken by the tobacco industry without delay. A marked reduction in the carcinogenicity of some of the major cigarette brands has already taken place. While such a move will not prevent smokers' developing lung cancer present evidence indicates that it will reduce the chances.

Wynder and his group are currently engaged in a study of the action of a number of substances, including aluminum compounds, to determine whether the temperature of tobacco during smoking can be lowered sufficiently to influence the formation of polynuclear substances. Several suggestions have been made for cooling the main stream of the smoke. The formation of carcinogens is related to the burning temperature rather than to the presence or absence of oxygen. Thus the activity of an 880 C tobacco pyrolysate in nitrogen is similar to that obtained with access of oxygen, but if the temperature is reduced below 700 C the carcinogenicity is reduced. Wynder is investigating the effect of catalysts on the reduction of the polynuclear content of tobacco smoke condensate. These studies are in the preliminary stage and it remains to be determined through combined biological and chemical investigations whether there is a particular catalyst or group of catalysts which could reduce the carcinogenicity of tobacco smoke and still be practical.

Hospital Leadership.—The main conclusion of a survey of hospital organization and administration in the past 10 years, made by the Acton Society Trust, entitled "Creative Leadership in a State Service—a General Survey," is that the Ministry of Health, while handling its administrative tasks fairly and sensibly, does not yet offer inspiring leadership to the decentralized authorities. Considering how such leadership might be provided Sir George Schuster, chairman of the trustees and himself chairman of a regional hospital board, discussed staffing of the Ministry, liaison between Ministry and regional boards, and provision of a central intelligence organization.

The creation of the National Hospital Service has resulted in the need for a new type of skilled medical administrator. Sir George believes that the Hospital Service could learn from both military organization and industry. The heads of hospital boards, for instance, should be able to expect from the Ministry of Health the leadership and direction which Army commanders would get from their commander-in-chief. From his own experience, Sir George repudiates the suggestion that the voluntary boards and committees, which are a unique feature of the British Hospital Service, are less concerned to insure the wise handling of funds than paid professional administrators would be. He would like to see economies effected not through progressive squeezing by the Ministry, but rather through expert study of the hospital cost structure, the use of efficiency techniques and industrial consultants, and the introduction of work-study methods. The survey is the subject of an editorial in the *British Medical Journal* of Feb. 14.

Children in Hospital.—Children should not be admitted to hospital if it can be avoided, according to an expert committee which made a two-year study of the arrangements for children in hospital. The committee, under Sir Harry Platt, found that at any given time in England and Wales there were nearly 40,000 children in hospital. Medical advance, said the committee, is making it possible to treat more children at home and so avoid the emotional disturbance caused by removing them from familiar environments. Greater attention should be paid to the emotional and mental needs of the child in hospital. The authority and responsibility of parents and the importance of mitigating the effects of the break with home should be more fully recognized. There is much to be said for admitting mothers with their children, especially if the child is under 5 years of age. Parents should be allowed to visit whenever they can and to help with the care of children.

The child should be allowed to take his favorite toys with him. Neither parent nor hospital should prevent his bringing something he loves on the grounds that it is not clean or respectable enough. The committee recognized the difficulty parents have in getting authoritative information about their children's progress. There should be fixed times at which parents could get such information first hand. Children and adolescents should not be treated in adult wards. There should be a plentiful supply of toys and games. All children's wards need a playroom, preferably one visible to those in bed. Hobbies, such as gardening, painting, and handicrafts, should be encouraged. The child, particularly at first, should be handled by as few people as possible. He should be able to get to know his own nurse. The *British Medical Journal* for Feb. 14 commented favorably on the report.

Carcinogens from Bonfires.—The garden bonfire is a major source of the carcinogen benzpyrene, according to Prof. F. C. Pybus of Durham University. Smoke from one of these smoldering heaps examined recently contained 70 parts of benzpyrene per 1 million of free carbon. The concentration of benzpyrene in tobacco smoke is 0.2 ppm. In coal smoke it is 300 ppm. The 180 million tons of coal burnt in a year produced 2,500,000 tons of smoke, against 18,000 tons from the 111,607 tons of tobacco burnt, but the coal yielded 750 tons of benzpyrene, compared with 8 lb. from the tobacco smoked. The author concluded that 90% of cancer is caused by the benzpyrene and other carcinogens in Britain's atmosphere. Great Britain has the smokiest air on earth.

The Insane Criminal.—Treatment with new drugs has transformed some patients who have been dangerously insane for years. Selected patients, many of them murderers, have for several months been given chlorpromazine, perphenazine, or prochlorperazine. Of 180 women patients so treated 30 were formerly so violent that they were locked in their cells permanently except for spells of exercise alone. Today only two are in isolation. The others are well enough to mix with other patients, work, and even attend dances in the concert hall. In one of the cell blocks for the most dangerous male patients is a man who murdered a prostitute 16 years ago. Before drug therapy he was incoherent and made only animal-like noises and was so dangerous that he could not be left alone with anyone except experienced male nurses. Four men had to hold him down for his first series of injections. Within seven days he was asking for the drug in tablet form. In two weeks he was holding normal conversations and working with other patients.

Another murderer had been in isolation for 10 years. In 1956 he was allowed out of his cell as an experiment, and his first response was to kick a nurse in the face. Now, after treatment, he is well behaved. This does not mean that cured patients will be released wholesale. These patients may have to take these drugs for the rest of their lives to remain normal. At this stage they could not be trusted to continue the treatment voluntarily if they were released, but these results are a great relief to the overworked staff. Not only do these people behave rationally but they are ambitious to get well and for the first time they are cooperating in their treatment.

CORRESPONDENCE

THE BASIC MEDICAL SCIENCES AND THE RESIDENCY PROGRAM

At the recent 55th Annual Congress on Medical Education and Licensure the residency program was the subject of a panel discussion, led by Dr. Wright Adams. One of the few points on which there was unanimous agreement was the difficulty in providing instruction at the graduate level in the basic sciences as they apply to the practice of the individual specialties. The important contributions of the basic medical sciences to advances in medicine through research have long been recognized. It is now becoming increasingly apparent that daily practice in the various specialties requires the application of specific physiological and other basic principles. This is recognized by the American specialty boards in their individual brochures, where the inclusion of instruction in the basic sciences as a part of residency training is stressed. The practical difficulty lies in finding available time and personnel to conduct this part of the total training program.

There is no question that the integration of basic and clinical instruction during daily ward rounds and seminars is one of the most effective ways of presenting both types of information. When the resident can relate certain principles of electrolyte balance to the treatment of an individual patient, the principles remain fixed and their application is readily recalled in future similar situations. Yet this alone is now insufficient. In the undergraduate medical curriculum, approximately one-half the total instructional time is devoted to the basic sciences as they relate to all branches of medicine. After completion of an internship, the future specialist usually spends the remainder of his formal training period in a residency program in which attention is focused on the area where he will practice throughout his career. Nowhere in this total program is there an opportunity for the systematic presentation of the important facets of the huge, steadily growing literature in the basic sciences as they apply to his field of specialization. Only in the university hospitals, which include a relatively small proportion of the total approved residencies, is it generally possible to obtain more than occasional visits from an anatomist, biochemist, microbiologist, pharmacologist, or physiologist. In such institutions, the faculty members usually carry such heavy undergraduate teaching schedules and research programs that they have little time left for regular courses for the hospital residents. Further difficulty lies in attempting to find class hours which the residents themselves can attend, uninterruptedly, with reasonable regularity. These problems are compounded in the nonuniversity community hospital, where the pathologist is generally the only basic science specialist on the staff. Even if funds were available to add others, the shortage of trained physiologists and biochemists would limit the use of this solution to the problem.

Recognition of this situation led the Graduate School of Medicine of the University of Pennsylvania to modify its curriculum this year. In the past, the school has offered courses in 14 medical specialties, in which correlated teaching in the basic sciences and their clinical application was conducted throughout the full academic year. This year, each course has been divided into a four-month basic semester and a four-month clinical semester. During the basic semester (September to January), students in all the specialties take the 192-hour correlated basic sciences course, in which is presented a review by body systems of the current literature in the basic sciences. The remainder of the basic semester of each course is devoted chiefly to instruction in the basic sciences as they apply to the individual specialty, and to seminars, conferences, and assigned reading in which the application of the basic sciences to clinical problems is stressed. The basic semesters in the various specialties were designed particularly for incorporation into the residency programs of approved hospitals.

During the current year, the first since the inception of the new program, approximately 50 physicians were sent to the school by their hospitals for the basic semester, in addition to the 200 enrolled for the full academic year. Opinions vary as to whether incorporation of the basic semester is most valuable during the early or latter part of the residency period. In general, we have found that the majority of physicians prefer taking the course after completion of approximately one year of residency. At that time, they have acquired sufficient clinical experience to serve as a background to the instruction offered and they have developed a strong appreciation of the need for further knowledge of the basic sciences in their areas of specialization. On returning to their hospitals after completion of the semester, they should be qualified to add materially to the local teaching programs.

The second, or clinical, semester (January to May) in each specialty is devoted primarily to clinical application and practice. The content of each full academic year's course at the school is thus essentially the same as in former years. This is of particular advantage to physicians who wish to enter the specialties after several years of general practice, to medical officers of the armed forces, who qualify for assignment to full year's courses, or who have just completed a tour of active duty, and to qualified physicians from abroad who desire a full year's training in the United States. Courses in the dental specialties and in veterinary medical sciences are given only as programs of a full academic year or longer.

Since its founding 40 years ago, the graduate school of medicine has striven constantly to develop more effective means of improving training in the specialties through application of the basic sciences. The present two-semester plan provides a means by which all approved hospitals can participate actively in its program.

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THE NEPHROTIC SYNDROME

To the Editor.—The editorial on the nephrotic syndrome in The Journal (169:846 [Feb. 21] 1959) disturbs us since we are sure it will confuse many readers. It quotes two references by ourselves and our co-workers which deal with the nephrotic syndrome. The other reference is a paper by Hodges (*J. M. Soc. New Jersey* 54:11 [Jan.] 1957) which deals with the lower nephron syndrome—so-called lower nephron nephrosis or acute tubular necrosis. Since there is no clinical and pathological similarity between these two conditions, and treatment is completely different, the editorial is confusing and misleading. In discussing the nephrotic syndrome, the editorial states that "pathologically the characteristic lesion is necrosis of the tubules." This lesion is seen in lower nephron nephrosis but not in the nephrotic syndrome. There are no characteristic histological lesions in the kidneys of patients with nephrotic syndrome. This condition has many causes and many renal histopathological changes but certainly not tubular necrosis. Other points discussed in the editorial confuse lower nephron syndrome with the nephrotic syndrome. For example, we have never heard of the artificial kidney being used in the treatment of patients with the nephrotic syndrome, but this form of treatment is valuable in the management of patients with acute renal failure due to the lower nephron syndrome.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Charitable Hospitals: Immunity from Tort Liability.—This was an action for damages sustained by a patient as a result of the alleged negligence of the defendant hospital. From an adverse judgment, the plaintiff appealed to the Supreme Court of New Jersey.

The plaintiff alleged that he entered the defendant hospital for the purpose of having an operation performed on his eyes. After the surgery he remained at the hospital as a postoperative patient and wore protective bandages over his eyes. During this postoperative period, and through the negligence of the defendant's employees in failing to provide suitable guard-railings on his bed, he was permitted to fall out of bed with great force and with resulting serious injuries. The defendant moved to dismiss the plaintiff's complaint, asserting that since it is a nonprofit eleemosynary corporation it possesses an absolute immunity from any responsibility to the plaintiff for injuries resulting from its alleged negligent conduct. The motion was granted and summary judgment entered in favor of the defendant.

The immunity on which the defendant relies, said the Supreme Court, was first declared in our courts in 1925 as a judicial expression of the state's public policy; however, the reasonable demands and expectations of innocent persons injured through the fault of others has caused many of our judges to suggest pointedly that sound concepts of right, justice, and morality require outright rejection of the immunity. In the case before us, the single issue presented by the parties is whether or not the last vestiges of the judicially declared immunity should at this time be erased.

The common-law duty of due care, with tort liability for its breach, prevails generally through the law although it occasionally comes into conflict with immunities which must find independent support for continued recognition in their own historical and social justification. Professorial and student writings overwhelmingly oppose the immunity of charitable hospitals. Although these writings are free from the restraints of judicial responsibilities, they are worthy of careful consideration for they embody thoughtful and high-minded endeavors to stimulate the movement of our law toward the ever-present goal of obtaining a higher measure of justice for all people.

Professor Scott has extensively discussed three possible grounds which have been suggested for the exemption of charitable institutions from tort liability. The first is that where trust funds are devoted to charitable objects they should not be diverted from those objects and that payment of tort claims would amount to such diversion, but this legalistic view would deny liability in all tort cases. The second rests on an alleged waiver by the injured party, but such a waiver would be wholly fictitious and a figment of the imagination. The third rests on the inapplicability of the doctrine of *respondeat superior*, but the adoption of this approach would deny liability in all tort cases and would seem to disregard the true ground for vicarious liability in our law. The New Jersey decisions did not really subscribe to any of the foregoing bases but spoke almost exclusively in terms of the public policy as the judges then saw it. Thus one Supreme Court decision recognized that the diversion of the charity's trust funds, if any, was the same whether the tort claimant was a beneficiary or stranger; and another, after finding the plaintiff to be a beneficiary, declared immunity as the state's declaration of public policy.

Times and circumstances have changed, however, the court continued, and we do not believe that some of these early decisions represent current notions of rightness and fairness. Due care is to be expected of all, and when an organization's negligent conduct injures another there should, in all justice and equity, be a basis for recovery without regard to whether the defendant is a private charity. We are satisfied that the views recently expressed in the concurring and dissenting opinions in two New Jersey cases are much closer to the mores and ethical ideals of our times than the earlier cases decided several decades ago. In one of these the court noted that experiences in other jurisdictions had demonstrated that no calamitous social effects would result from dissolution of the charitable immunity; that the availability of insurance had obviated any threat that recoveries against charities would seriously deplete their funds and deprive communities of their benefits; and that individuals "should not be forced to suffer the unmitigated and oftentimes crushing burden of injuries wrongfully inflicted merely to continue a judicially inspired immunity long since outdated by the impact of modern times." The other decision pointed to the harshness and injustice of the immunity rule and questioned any present need for it in view of the widespread availability of insurance. It may be noted that charitable institutions in New Jersey have long been under some tort responsibilities for negligent injuries to others and presumably have protected themselves by adequate insurance coverage; if the enlargement of their tort responsibilities actually results in additional premiums, that should be considered as merely incidental to the rendering of equal justice to all innocent parties who are injured through the negligence of others.

The contention has been advanced that, even though the former public policy notions have been strongly altered, the elimination of the immunity should be left exclusively to the legislature. Judges of an earlier generation declared the immunity simply because they believed it to be a sound instrument of judicial policy which would further the moral, social, and economic welfare of the people of the state. When judges of a later generation firmly reach a contrary conclusion they must be ready to discharge their own judicial responsibilities in conformity with modern concepts and needs. It should be borne in mind, the court pointed out, that we are not dealing with a field of the law in which stability and predictability may be of the utmost concern. We are dealing with the law of torts, in which there can be little, if any, justifiable reliance and where the rule of *stare decisis* is admittedly limited. We find no merit in the defendant's contention that "this court may not constitutionally overturn the immunity doctrine." It seems to us beyond question that, in the absence of any definitive legislative public policy, this court has full power to overrule the earlier declaration of court of error and appeals either because it was originally erroneous or because it has become unsound in the light of modern conditions. Since earliest days our courts have recognized and discharged the vital responsibility of reexamining questioned decisions whether they be their own or those of their predecessors.

The primary function of the law is justice, and when a principle of the law no longer serves justice it should be discarded. In this case the law was embodied not in any controlling statute but in a judicial principle of the law of torts; it had no sound English common-law antecedents and found its way into American law through a misconception; it runs counter to widespread principles which fairly impose liability on those who wrongfully and negligently injure others; it operates harshly and disregards modern concepts of justice and fair dealing; it has been roundly and soundly condemned here and elsewhere; and the time has come for its elimination by the very branch of government which brought it into our system.

Since the dismissal of the plaintiff's complaint was grounded entirely on the defendant's alleged immunity which we now repudiate, concluded the Supreme Court, the judgement in favor of the defendant is reversed and a new trial ordered. *Collopy v. Newark Eye and Ear Infirmary,* 141 A(2) 276 (N. J., 1958).

Malpractice: Res Ipsa Loquitur; Failure to Pretest for Possible Drug Reaction.—This was an action for damages for injuries caused by the alleged negligence of the defendant physician. From a judgment in favor of the defendant, the plaintiff appealed to the district court of appeals, first district, division 1, California.

The plaintiff was referred by her regular physician to the defendant for a pyelogram, an x-ray study of the urinary tract. It is accomplished by the injection of an opaque iodine dye so that the inside of kidneys, ureters, and bladder can be photographed. The plaintiff testified that the defendant did not make any reaction tests and did not ask her whether she usually had reactions to injections or was sensitive to any particular substance. The defendant insisted that she did ask the necessary questions and that she did make an intradermal sensitivity test. On attempting to make the injection in the right arm, then the left arm, and finally in the veins of one of the wrists and hands, it was found that the plaintiff's veins were friable and had started to bleed. (During these unsuccessful attempts the defendant used about 10 cc. of the dye. Not all of it got into the plaintiff's veins but the defendant observed no adverse reactions to the amount that did.) Defendant therefore told the patient that the injection could be made in either the shoulders or the buttocks and the plaintiff chose the buttocks. After administering Novocain to deaden the pain the defendant proceeded to inject about 30 cc. of Neo-iopax. She admitted that Neo-iopax is an irritant, but she did not warn the patient that there might be a reaction because she did not expect one, never having observed one before. It appeared from the evidence that the manufacturer's comments about Neo-iopax indicated that it was to be used "for intravenous and retrograde urography" but made no mention of intramuscular injections. The defendant stated, however, that it was common practice in the community to inject it intramuscularly if it could not be injected intravenously.

Immediately after injection of the dye, the plaintiff experienced severe pain. An ulcer developed at the site of the injection which subsequently required surgery before it cleared up.

The plaintiff's main contention was that the doctrine of *res ipsa loquitur* applied. It is very doubtful, said the court of appeals, that the doctrine is applicable to the facts of this case. Whether the doctrine is applicable depends upon whether a layman can say, as a matter of common knowledge or observation, or from the evidence could draw a reasonable inference, that the consequences of the injection here involved were not such as ordinarily would have followed if due care had been exercised. In this case the injury arose at the site of the injection. The testimony of the various doctors was all to the effect that it is good and standard practice in this community to give such an injection subcutaneously if it cannot be given in the veins. The defendant testified as to why it was not possible or feasible to give this injection to the plaintiff intravenously. Thus, there is no basis at all for the plaintiff's assertion that there was an inference of negligence because the injection was here given subcutaneously. All the testimony is to the effect that the reaction here involved is one of the risks of such an injection. Such toxic effects are caused by the sensitivity of the individual patient to the dye solution. There would seem to be no basis for the doctrine of *res ipsa loquitur.*

We think, however, continued the court of appeals, that there was substantial evidence, independent of the doctrine of *res ipsa loquitur,* to support a verdict for the plaintiff. The defendant testified that she asked the plaintiff about her reactions to injections and made tests for sensitivity. Although she was skeptical about the value of such tests, the fact remains that the defendant claimed that she made such tests and asked the relevant questions. It is certainly a possible and reasonable inference from the defendant's testimony that the giving of such tests and the asking of such questions were common and standard procedure in this area. But the plaintiff testified that no such tests were given and no such questions asked. Thus, there is a direct conflict in the evidence on the vital issue of negligence. It is a reasonable inference from the evidence, and the jury could have found, that ordinary care required the giving of such tests and the asking of such questions. The jury could then find that it is negligence to fail to give such tests or to fail to ask such questions. Finally, the jury could have found that no such tests were given and no such questions asked by the defendant. Thus, there was a factual issue that should have been submitted to the jury.

The judgment of the trial court in favor of the defendant physician was accordingly reversed. *Horace v. Weyrauch,* 324 P(2) 666 (Calif., 1958).

Malpractice: Careless Remarks by Operating Surgeon.—This was an action for damages for injuries caused by the alleged negligence of the defendant surgeon. From a judgment of nonsuit, the plaintiffs appealed to the district court of appeals, third district, California.

The patient entered the St. Helena Sanitarium and Hospital for the purpose of having a rectosigmoid polyp removed from the lower portion of the large intestine adjacent to and immediately above the rectum by the defendant surgeon. After such an operation it is customary to examine the site of the polyp in order to ascertain whether or not the entire polyp has been removed. There was an attempt to make this examination just before the plaintiff left the hospital, but because of the pain caused to the plaintiff it was decided that the examination would be made at a later date and with the plaintiff under an anesthetic. Subsequently, therefore, the plaintiff returned to the hospital. She was given a general anesthetic, and a sigmoidoscope was inserted up her rectum without difficulty to the 15-cm. level. At this point the obdurator was removed because the defendant desired to pass the scope under direct vision. In attempting to advance the sigmoidoscope under direct vision slight difficulty was encountered, and on visual examination it was noted through the scope that a loop of the small intestine was visible. A diagnosis of accidental perforation of the sigmoid wall was made, and the plaintiff was immediately taken to the operating room where abdominal repair was performed.

The plaintiff husband testified that when the defendant came out of the operating room he approached him and said, "Boy, I sure made a mess out of things today, didn't I, Warren?" Asked what happened, he replied, "Well, by inserting my scope in your wife's rectum, I busted the intestine."

The defendant testified that a tear of the intestine is not an expected or anticipated thing and that he was totally unaware that the intestine had been torn until "it was noted that loop of the small bowel was visible."

The plaintiffs first contended that a judgment of nonsuit was not proper because of the application of the doctrine of *res ipsa loquitur*. The court held that the doctrine would not apply in the instant case unless it was shown that the accident was one that does not ordinarily occur in the absence of negligence. We cannot say, the court continued, that it is a matter of common experience that a rent in the intestine does not occur during a sigmoidoscopy in the absence of negligence. Expert testimony would be required. The only evidence introduced in this regard was a statement of the defendant that a tear is not anticipated or expected. The mere fact that the result is unexpected or not anticipated is not sufficient to invoke the doctrine of *res ipsa loquitur*.

The plaintiffs also contended that the extrajudicial admission of the defendant was sufficient to establish a prima facie case. The court said that on the issue of nonsuit the plaintiff was entitled to all favorable inferences that could reasonably be drawn from the evidence. What inferences were to be drawn from the defendant's statements, in the light of the facts and circumstances shown by the evidence, was a question of fact to be determined by the jury. We believe that the court erred in determining as a matter of law that no inference of negligence could be drawn from the evidence. We think that the jury could infer from the statement that in inserting the sigmoidoscope he did not use the degree of care ordinarily exercised by other doctors of good standing in the community, and, as a result of the lack of care, the patient's intestine was torn.

Accordingly the judgment of nonsuit in favor of the defendant surgeon was reversed. *Wickoff v. James,* 324 P(2) 661 (Calif. 1958).

Malpractice: Abandonment of Patient.—This was an action for damages resulting from the alleged abandonment of the plaintiff by the defendant physician after having accepted him as a patient. From a judgment in favor of the defendant, the plaintiff appealed to the court of appeals of Georgia.

After a traffic accident the plaintiff was taken to a hospital in Carrolltown, Ga., and from there to the Georgia Baptist Hospital, Atlanta, where the defendant was shown by the hospital charts to be the admitting physician. The plaintiff suffered a fractured left mandible, a fractured zygomatic bone, at least two fractured ribs, fractures of the vertebral column, and a fractured skull. After five days the plaintiff was removed to his home where the defendant saw him weekly for about four weeks, until he advised the plaintiff that he would have nothing further to do with the case. The plaintiff then consulted an attorney to force the defendant to furnish him proper treatment. At the time of the trial the plaintiff still suffered from some of the injuries, and he contended that he had been unable to procure medical treatment since the defendant "abandoned" him.

The plaintiff testified that the defendant told him on March 21 that he would not get well until he obtained surgical treatment but that he, the defendant, would not take care of him. The plaintiff also testified that another physician treated him several times up to March 18, when he said he was going to place him in a hospital.

There was no evidence, said the court, that the defendant abandoned the plaintiff at a critical time when there was a need for immediate treatment, for, although the record does disclose that the plaintiff needed surgical treatment, it does not disclose that such surgical treatment was needed then and there or that if the plaintiff had sought, within a reasonable time thereafter, other medical care he would have suffered any injury from the alleged abandonment. It is undisputed that the day after the alleged abandonment the plaintiff traveled from his home to Atlanta where, at the request of his attorney, he was examined by a physician who recommended that he see a plastic surgeon. It appears that any injury which the plaintiff suffered resulted from his own failure to obtain the treatment recommended for him.

The judgment for the defendant physician was therefore affirmed. *Carroll v. Griffin,* 101 S. E. (2) 764 (Ga., 1958).

MEDICAL FILM REVIEWS

No Man Walks Alone: 16 mm., black and white, sound, showing time 27 minutes. Presented as a public service by the National Paraplegia Foundation Inc., New York. Produced in 1958 by and procurable on rental ($12.50) or purchase ($150.00) from Film Features Inc., 1600 Broadway, New York 19.

This film deals with new developments in the physical rehabilitation of a paraplegic patient. It shows the experiences of a patient from the time he begins treatment for a broken back through his training and adjustment and finally his preparations for work. The teamwork of the hospital staff of physicians and therapists who help the paraplegic patient back to useful living is also shown. It is suitable for showing to lay groups and could also be used for fund raising purposes

Positioning the Patient for Surgery: 16 mm. color, sound showing time 27 minutes. Presented by the American Nurses Association and National League for Nursing Film Service in cooperation with the American College of Surgeons. Produced in 1958 by and procurable on loan from American Cyanamid Company, Surgical Products Division, 1 Casper St., Danbury, Conn.

This film demonstrates how the operating room nurse fulfills her responsibility for proper positioning of the patient on the operating table and performs those activities which help to maintain physiological functioning, conserve time and energy, prevent bodily injury, and provide for the comfort and dignity of the patient. The positions shown are dorsal recumbent with one arm abducted, Trendelenburg, lithotomy, lateral, and prone. The safety and physical comfort of the patient are emphasized, and the film shows evidence of good planning. The film might also have demonstrated the importance of talking with the patient and reassuring him, in those cases where he is positioned prior to the induction of anesthesia, but this is a minor criticism. The photography is good, and the film could be shown to nursing students who are having their first experience in the operating rooms. It could also be shown to graduate nurses, either in an orientation program planned for the operating room or in a postgraduate course of study.

Transporting the Patient for Surgery: 16 mm., color, sound, showing time 15 minutes. Presented by the American Nurses Association and the National League for Nursing Film Service in cooperation with the American College of Surgeons. Produced in 1958 by and procurable on loan from American Cyanamid Company, Surgical Products Division, 1 Casper St., Danbury, Conn.

This film demonstrates the coordinated responsibilities, interdepartmental and intradepartmental, of the hospital in providing safe transportation for the patient. Those concerned are the operating room nursing staff, the anesthesiology staff, and the nursing staff assigned to the patient unit. The method of procedure may vary with the facilities available in a hospital; however, the basic principles of safe transportation are applicable. An especially good feature of this film is its emphasis on the nurse identifying the patient and assisting him to the stretcher bed. The actress playing the nurse in the recovery room has an especially pleasant expression and conveys a feeling of genuine interest in the patient. The safety and comfort of the patient are correctly emphasized, and the photography is good. The narration is rather monotonous, but the content of the description is good and the narrator does not appear to be reading. The film is recommended for showing to student and graduate nurses and also to aides and orderlies.

Al in the Hospital: 16 mm., black and white, sound, showing time 22 minutes. Produced in 1950 by and procurable on purchase ($120) from Robert Disraeli Films, 206 E. 17th St., P. O. Box 343, Cooper Station, New York 3.

The story begins in the classroom where Al's chair is empty because he is in the hospital. His classmates write him a letter which the teacher delivers. At the request of his classmates Al makes drawings of his experiences. He tells about the bicycle accident which resulted in a broken leg and explains about x-rays, his cast, and the daily hospital routine. Hospital procedures such as a blood test and an injection are shown. Most of the film is narrated by a boy about 8 years of age and would appeal to children of this age group. Its purpose is to allay the fears of children who might be hospitalized; however, only the pleasant things are shown such as the competent nurse's care and the play room. The film is rather long, but it should be useful for showing to children and their parents.

Stapes Mobilization and Fenestration of the Oval Window for Otosclerotic Deafness: 16 mm., color, sound, showing time 21 minutes. Prepared by Samuel Rosen, M.D., New York. Produced in 1958 by Sturgis Grant Productions, New York, and procurable on loan from Samuel Rosen, M.D., 101 E. 73rd St., New York 21.

The surgical procedures of mobilization and fenestration are adequately explained in this film by drawings and diagrams and beautifully demonstrated by pictures of the actual surgery. The presentation of the anatomy, physiology of the conducting mechanism, and pathology of stapes ankylosis in the film is too brief for teaching purposes, and its value would be enhanced if more time were given to presentation of the problem. Some reference to the history of "mobilization of the stapes" and results obtained by this procedure before the turn of the century would also heighten the teaching value.

The three stages or types of operation used by the author are clearly demonstrated. The advisability of the first and third types of operation, however, is open to question in the light of the experiences of others. The first type has been discarded by many surgeons because of the danger of fracturing the crura. Also, there have been occasional injuries to the facial nerve in the hands of unskilled operators. The third procedure, fenestration of the foot plate, has been objected to by some surgeons because of failure to obtain useful hearing improvement, rapid loss of any hearing gain obtained, and possible increase in danger of injury to the inner ear. The explanation offered in the film for the gain in hearing from the third procedure is obviously deficient and does not agree with known facts concerning the effect of interruption of the ossicular chain on the hearing of air-conducted sound. Although the conditions which occur here have never been exactly duplicated, it appears that there is some clinical evidence to support the claim that improvement in hearing can be obtained by fenestration of a fixed stapes with the drum membrane intact. Further evidence is needed, however, in order to assess definitely the value of this procedure and either corroborate or disprove the claims made by the author.

The presentation of the problem for which this type of surgery is carried out is inadequate and should be improved, if the film is to be of optimum value in general medical teaching. The photography and recording of the actual surgical procedures are excellent, even though the scientific validity of the interpretations leaves something to be desired. It would have been preferable to indicate clearly that the hearing improvement from fenestration of the foot plate is not yet completely understood.

A Complete Office Gynecological Examination: 16 mm., color, sound, showing time 16 minutes. Prepared by Frederick J. Hofmeister, M.D., Milwaukee. Produced in 1958 by and procurable on loan from Frederick J. Hofmeister, M.D., 2212 W. State St., Milwaukee.

This film demonstrates the author's concept of what constitutes a complete gynecologic examination, and it emphasizes the fact that this must be a complete physical examination and demonstrates the examination of the breasts as an essential phase. Examination of the genitalia includes the Papanicolaou smear, endometrial biopsy, rectovaginal-abdominal examination and, where necessary, a cervical biopsy (which is demonstrated). Breast examination and the various methods of smear and biopsy for both cervix and endometrium are correctly shown. The photography is excellent and the film is recommended for postgraduate teaching of physicians, medical students, and nurses.

A Technique for Measuring Minimal Social Behavior: 16 mm., color, sound, showing time 12 minutes. Produced in 1957 by and procurable on loan from Veterans Administration, Central Office Film Library, Washington 25, D. C.

This is a filmed record of a schizophrenic patient being subjected to a newly devised psychological test. The procedure consists of observing the manner in which he enters the psychologist's office, picks up an ostentatiously dropped pencil, accepts a cigarette or a diagram of a crossed square, answers questions as to his orientations for time and place, and finally responds to a rather abrupt dismissal. The technique of scoring all this is not explained, but we are assured that the results differentiate specific degrees of "minimal social behavior." To an experienced viewer it might seem that the aloof, stereotyped, coldly inquisitorial method employed could well contribute to keeping the subject defensively withdrawn and autistic; perhaps deliberately, no attempt is made to explore his capacity to respond to human warmth or individualized communication. Possibly for the latter reason, some whimsical producer chose a musical background which uses themes derived mainly from Dukas' "The Sorcerer's Apprentice." The film is recommended only to those interested in a comparative study of psychological test procedures rather than in more searching samplings of normal and aberrant conduct.

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

The following films were produced in 1958 as a public service by the Sears Roebuck Foundation in cooperation with the American Hospital Association and the University of Illinois Research and Educational Hospitals. All are in 16 mm., color, and sound. Procurable on loan (service charge $2.00 each) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., *Chicago 10.*

RX–A Prescription for Better Hospital Procedures
Showing time 25 minutes
The Flow Process Chart as Applied to Hospital Activities
Showing time 20 minutes
The Questioning Attitude as Applied to the Flow Process Chart
Showing time 19 minutes
The Right and Left Hand Chart as Applied to Hospital Activities
Showing time 23 minutes
Motion Economy as Applied to Hospital Activities
Showing time 22 minutes

This series of films is a clear demonstration of the method of planning and inaugurating a work simplification program. It illustrates some of the myriad hospital routines susceptible to such a program and should find application to other related medical centers such as clinics or other types of offices with multiple health programs and procedures. The most impressive thing about this series of related films is that they were made with actual participants in the programs instead of professional actors. An important feature of the series is that it highlights the method of attack and illustrates the results with several lucid examples. Since work simplification is a continuing responsibility of overworked medical personnel, these films should afford a provocative stimulus on a "do it yourself" basis.

(Note: The first film in the series—RX–A Precription for Better Hospital Procedures—was reviewed in THE JOURNAL of April 26, 1958, p. 2216.)

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Etiology of Hyperostosis Cranii (Metabolic Craniopathy): A Clinical Study. J. E. Caughey. J. Bone & Joint Surg. 40B:701-721 (Nov.) 1958 [London].

Hyperostosis cranii or metabolic craniopathy is a syndrome characterized by thickening of the inner table of the skull, which is more usual in the frontal region but may also occur over other parts of the skull, including the basal bones and the orbital plate. There may be generalized thickening of the whole cranium. In the frontal region especially the inner surface of the skull may become nodular, and it may attain a depth of ½ in. (1.27 cm.). This thickening consists of spongy bone containing large numbers of osteoblasts, and the underlying dura is usually thickened and adherent. A review of the literature has revealed that hyperostosis cranii is associated with several clinical states, such as the Stewart-Morel syndrome, acromegaly, and dystrophia myotonica, and it may also occur as "senile hyperostosis." Most workers who have studied the syndrome of hyperostosis cranii have noted the overwhelming occurrence among women. Dystrophia myotonica, a heredofamilial disorder of which hyperostosis cranii is one of the variable and common features, however, occurs equally among men and women. In a small but convincing series of cases of dystrophia myotonica, hyperostosis cranii was also found distributed equally among men and women.

The causation of hyperostosis is still a matter for speculation. More recent studies have focused attention on the endocrine system, and it seems probable, in view of the sex distribution in dystrophia myotonica, that the key to the problem may be found in this disorder. The author studied 50 patients with fully developed dystrophia myotonica, and the cases of 9 of these patients belonging to 6 families are reported in detail. The characteristic skull changes in these patients were hyperostosis cranii, a small pituitary fossa, excessive sinus formation, and prognathism. These changes in the skull may be described as acromegaloid. Gonadal atrophy was a common feature, and endocrine studies suggested that the endocrine defect is primarily a failure of the androgenic function of the adrenals and the testes. In rodents and in man ablation of the gonads leads to overactivity of gonadotrophic cells and, at times, of somatotropic cells. Sometimes pituitary tumors develop. Acromegaloid features may occur in eunuchs, and it is likely that the acromegaloid changes in patients with dystrophia myotonica are of the same order from overactivity of growth hormone. In animals excess of growth hormone produces thickening of the skull. In dystrophia myotonica, acromegaly, and the Stewart-Morel syndrome it is suggested that hyperostosis cranii is an expression of unrestrained activity of growth hormone.

Reduction of Serum Cholesterol in Hypercholesteremic Patients: Effect of a Polysorbate 80-Choline-Inositol Complex. H. L. Fuller. Maryland M. J. 8:6-13 (Jan.) 1959 [Baltimore].

The difficulty in controlling hypercholesteremia by diet alone indicates that some adjunct to diet would be of value. A number of agents have been studied and proposed for the control of hypercholesteremia. Among these are lecithin, lipotropic agents, estrogenic substances, vitamin B factors, pyridoxine, nicotinic acid, plant sterols, beta-sitosterol, vitamin E and wheat germ oil, polysorbate 80 complex, and unsaturated fatty acids. The author undertook the study of a polysorbate 80 complex in the management of hypercholesteremic patients. Patients were chosen from private clinical practices, general hospital outpatient departments, and chronic geriatric institutions. The subjects were known either to be obese or to have cardiovascular and peripheral vascular disease, diabetes, and hypothyroidism (idiopathic or postoperative myxedema). The serum cholesterol levels were determined. Of the 200 patients screened, 41 were selected who had serum cholesterol levels over 300 mg. per 100 cc. Their cholesterol values ranged from 300 to 1,460 mg. per 100 cc. Seventeen were women, and 24 were men. Their ages ranged from 33 to 66 years. The diabetics included in the study were well controlled, and their diet was deliberately unchanged while they were under observation. The hypothyroid patients maintained an euthyroid state with adequate doses of thyroid hormone. The patients with cardiovascular disease were all in

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The place of publication of the periodicals appears in brackets preceding each abstract.

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fairly good state of health, without evidences of congestive failure or histories of previous thromboembolic phenomena or vascular accidents. Rigid dietary restrictions had failed to induce significant reduction of serum cholesterol levels.

After determining the fasting serum cholesterol levels on 2 separate occasions, a week apart, treatment with polysorbate 80-choline-inositol complex (Monichol) was begun. The mixture was administered in doses of 10 cc. twice daily, and in some patients it became necessary to increase the intake to 40 cc., or even 60 cc. in 24 hours. All patients experienced a significant fall in serum cholesterol; in general, the higher the initial level, the greater the reduction achieved. Normal cholesterol levels could be maintained only by uninterrupted continuance of therapy. A sense of well-being was described by many of the patients. No significant side-effects were encountered. The long-range effect of reducing hypercholesteremia, particularly with respect to the possibility of reducing arterial disease, remains to be established. In a patient with cholelithiasis of the cholesterin variety, the stones were observed to dissolve during the period of treatment with Monichol. The author feels that possibly the medication in conjunction with a rigid low-fat, low-cholesterol diet, administered for the purpose of weight reduction, was the answer, since 2 other women, with shadows in their cholecystograms, who were not placed on restricted diets, did not experience stone resolution. Further studies on this problem are now in progress.

Hemodynamic Effects of Atrial Fibrillation in Patients with Mitral Valvular Disease. B. Caini and M. M. Brunori. Sett. med. 46:395-401 (Sept. 30) 1958 (In Italian) [Florence, Italy].

Hemodynamics were studied in 80 patients with mitral valvular disease, 30 of whom had atrial fibrillation and the remainder sinus rhythm. Pulmonary arterial pressure was, on the average, lower in patients with atrial fibrillation than it was in those with sinus rhythm; it rose gradually and in proportion to the increasing degree of physical disability in patients with sinus rhythm. There was no significant difference in increased pulmonary arterial pressure among patients with atrial fibrillation and a high rate of physical disability, such as those in groups 3 and 4 according to the American Heart Association classification. The discrepancy in pulmonary arterial pressure among patients with atrial fibrillation of groups 1 to 4 (American Heart Association classification) was also less pronounced than it was among patients with sinus rhythm. Pulmonary capillary pressure was lower in patients with atrial fibrillation than it was in those with sinus rhythm. No patient with atrial fibrillation had a capillary pressure above 25 mm. Hg. Blood pressure within the right atrium in patients with atrial fibrillation was higher than it was in patients with sinus rhythm. The degree of dilatation of the left atrium in patients with atrial fibrillation was distinctly greater than it was in those with sinus rhythm. Thus, atrial fibrillation, which developed in the course of mitral valvular disease, has appreciably changed the hemodynamic state in this series of patients; it relieved the pulmonary hypertension but increased the hypertension in the right atrium and in the venous branch of the systemic circulation.

Thymoma and Hemopoietic Insufficiency. E. R. Fisher and F. D. Beyer Jr. A. M. A. Arch. Int. Med. 103:95-104 (Jan.) 1959 [Chicago].

The authors point out that the association of thymic neoplasms with myasthenia gravis is well recognized, but that the exact nature of this association is not clear. In recent years attention has been directed to the occurrence of thymic tumors in several other clinical disorders, notably hypoplastic anemia, agammaglobulinemia, and pituitary basophilism (Cushing's disease). This report describes the clinical and pathological features of a 68-year-old man, in whom a thymic neoplasm was associated with severe hypoplasia of the bone marrow and pancytopenia. Sixteen previously recorded cases of the association of a thymic neoplasm or hyperplasia and hemopoietic insufficiency are reviewed. Although absolute proof that the latter is directly caused by the thymic neoplasm is lacking, certain considerations suggest such a relationship.

In at least 2 previously reported instances, the thymic neoplasm clearly antedated the blood dyscrasia. Improvement in hemopoietic function was observed in 5 of the 8 patients in whom a thymoma was successfully resected. The failures after thymectomy do not necessarily refute the significance of this observation. It is conceivable that irreparable marrow changes may occur, preventing a satisfactory response. The delayed response observed in several instances suggests that death may result from intercurrent causes before sufficient time has elapsed for marrow regeneration. It is worthy of consideration that in some instances thymic remnants were overlooked at the time of operation. This possibility suggests that the thymus per se may be influenced by its neoplastic component to produce such an effect. Lastly, rarity of both thymoma and idiopathic hypoplasia of the bone marrow would suggest that their association is more than one of chance. The failure to obtain in the patient presented a history of exposure to chemical poisons or to find clinical or pathological evidence of hypersplenism, endocrine disorder, or hemolytic anemia substantiates the primary nature of the hemopoietic disorder encountered. The relatively small amount of irradiation received by this patient appears insufficient to have produced such an effect.

Pathological classification of thymic neoplasms is unsatisfactory, and the relatively noncommittal term "thymoma" has gained popularity. However, the association of these neoplasms with various disease states suggests that attention should be directed to morphologic variants in thymomas. Review of the previously recorded examples of thymoma associated with refractory anemia or pancytopenia, in which sufficient morphologic information was available, revealed the spindle-cell type of thymoma to be most frequent in this syndrome. The lesion in the patient of this report was also of this type. Attention is directed to the histological similarities of the spindle-cell thymoma and hemangiopericytoma.

Some Less Familiar Roentgen Manifestations of Intrathoracic Histoplasmosis. B. Felson. A. M. A. Arch. Int. Med. 103:54-62 (Jan.) 1959 [Chicago].

After the demonstration of close correlation between histoplasmin skin sensitivity and intrathoracic calcification in the population of the Ohio and Mississippi river basins, it was predicted that active histoplasmosis would be recognized with increased frequency. This prediction appears to have materialized. For the most part the roentgenologic manifestations of intrathoracic histoplasmosis fall into the following 3 main categories: (1) an acute disseminated form with miliary or small patchy densities diffusely distributed throughout the lungs, sometimes encountered in epidemics, (2) a localized pneumonic form, and (3) the solitary nodule ("coin" lesion, histoplasmoma) of chronic and asymptomatic nature. Each of these types may be associated with hilar and/or mediastinal lymph node enlargement, the so-called primary complex. The healing phase is commonly accompanied by the deposition of calcium in the pulmonary lesions and lymph nodes, though complete clearing of the lungs without calcification is not unusual. The persistent spherical focus, or histoplasmoma, may represent either the end-result of an earlier pneumonic infiltrate or a filled-in cavity and is generally considered inactive. It often contains a solid or laminated central core of calcification, best demonstrated by tomography.

In discussing some less familiar manifestations of histoplasmosis, the author first takes up fibrocavitary histoplasmosis, which was observed in his department at the University of Cincinnati College of Medicine and the Cincinnati General Hospital in 5 patients, who ranged in age from 38 to 76 years. Each had been hospitalized in a tuberculosis sanatorium, where the correct diagnosis was established. A positive histoplasmin skin test was found in 4 cases, and a positive tuberculin test in 3. The histoplasmin skin test is important if Histoplasma capsulatum is not found in the sputum. That the process was essentially fibrotic in nature was evident from the duration of the disease, the irregular, dense, and sometimes linear appearance of the infiltrate, and the contraction of the thorax with retraction of the hilar and mediastinal structures. Extensive cavitation was present in all cases. The cavities were generally large and multiple. In 3 patients the lesions progressed, in 1 they remained stationary, while in 1 marked regression occurred.

Another less familiar roentgenologic manifestation of histoplasmosis is enlarging histoplasmoma. This form is rare, since the vast majority of histoplasmomas remain unchanged over prolonged periods of observation, probably representing a spent form of histoplasmosis. Broncholithiasis, a sequel of long-standing histoplasmic lymphadenitis, is not so rare in the Cincinnati area, at least 12 cases having been observed in the past 5 years. Other sequelae of prolonged histoplasmic lymphadenitis are traction diverticulum of the esophagus, multiple histoplasmomas, the middle-lobe syndrome, and superior vena caval obstruction, the latter resulting from fibrous or calcific mediastinitis. In the endemic area histoplasmosis must be given serious consideration in all instances in which a diagnosis of pulmonary tuberculosis was formerly entertained.

The Varied Clinical Manifestations of Coxsackie Virus Infections: Observations and Comments on an Outbreak in California. R. B. Gordon, E. H. Lennette and R. S. Sandrock. A. M. A. Arch. Int. Med. 103:63-75 (Jan.) 1959 [Chicago].

The known Coxsackie viruses have been placed in 2 different groups on the basis of histopathological changes produced in the mouse. At the present time, there are at least 19 immunologically different viruses within group A and 5 immunologically different types within group B. The authors discuss epidemiologic and clinical observations incident to a large outbreak of Coxsackie virus infection in California, which was first recognized in and around Shasta County in the summer and fall of 1956. The outbreak was primarily one of pleurodynia, but cases of aseptic meningitis and of pericarditis and pleural effusion were also encountered. As far as the authors are aware, this is the first time that Coxsackie virus, group B, type 5 has been reported as a cause of epidemic pleurodynia. The Coxsackie group B viruses have previously been incriminated as a cause of myocarditis in infants. These viruses are now also incriminated as etiologically responsible for some cases of acute benign pericarditis. The data presented in this report show that infection with a single immunological type of Coxsackie virus, namely, group B, type 5, can give rise to a variety of clinical manifestations, such as epidemic pleurodynia, aseptic meningitis, pleurodynia with meningeal involvement, pericarditis, and, very probably, myocarditis.

Effect of Prednisone on the Capillary Permeability in Patients with Heart Disease Associated with Edema. F. Fontanini, P. L. Prati and A. Rivi. Sett. med. 46:401-405 (Sept. 30) 1958 (In Italian) [Florence, Italy].

The authors investigated the existence and the intensity of a possible property of prednisone to control capillary permeability, besides the known diuretic effect, in the course of its administration to patients with heart disease accompanied by decompensation. Fifteen patients with chronic insufficiency of circulation associated with edema received prednisone in daily doses of 0.5 mg. per kilogram of body weight for 5 days. Before the treatment began, an excessive transudation of fluid through the capillary walls was present in 10 patients and an increased loss of protein substances at stasis in 13. Permeability of fluid and of proteins was restored to almost normal values in most patients and was improved in the others. A better effect was observed on the capillary permeability of proteins than of fluid, because the loss of proteins was, on the average, slightly below the upper physiological limit, and the transudation of fluid was, on the average, slightly above that limit. Prednisone therapy in this series of patients corrected the anatomic functional disorder of the capillary permeability, regardless of the action of any hemodynamic mechanism. It is, therefore, an efficacious drug, used either alone or in combination with other cardiotonic drugs, in the treatment of patients with decompensated heart disease associated with edema, who become refractory to common therapeutic measures.

Time of Occurrence and Duration of Pain Periods in Patients with Duodenal Ulcers After Small Meals. H. J. N. Dekkers and J. W. Tjeenk Willink. Nederl. Tijdschr. Geneesk. 102:2368-2371 (Nov. 29) 1958 (In Dutch) [Amsterdam].

It is generally accepted that the pain of duodenal ulcer is the result of chemical irritation of the ulcer crater by peptic gastric juice or by hydrochloric acid. In earlier studies the authors had demonstrated that this pain occurs during evacuation of the stomach and not, as is widely assumed, when the stomach is empty, and that, therefore, the term "hunger pain" is not justified. They now describe studies they carried out on 139 patients with duodenal ulcers to ascertain the time and the duration of evacuation of the stomach after a small meal. Gastric evacuation was studied clinically in 98 patients and roentgenologically in 84. The test meal consisted of 70 Gm. of bread, 10 Gm. of butter, 30 Gm. of cheese, and 0.4 liter (about ¾ pint) of milk. Fractional titration of the stomach contents ascertained not only the emptying time but also the onset and duration of the pain periods. In 51 of the 84 patients who were subjected to roentgenologic examination, the emptying time of the stomach was measured first after only barium sulfate was given. Later all 84 patients were tested with a mixture of barium sulfate and the same type of food given for the clinical examinations.

The majority of the patients who were examined clinically required more than 5 hours to empty their stomachs; the majority of those studied roentgenologically required more than 6 hours, although barium sulfate alone had left the stomach in 3 hours. Periods of pain, when they did occur, commenced from 1 to 4 hours and ended from 3 to 5 hours after the meal in the clinically examined patients; they generally lasted from 1 to 2 hours. During the somewhat slower evacuation during the roentgenologic tests the duration of pain was more variable than during the clinical tests. In some of the roentgenologic tests the pain terminated more than 6 hours after the meal, but it still coincided with the evacuation. Pain never occurred after evacuation of the stomach was complete.

The Prognostic Value of Leukocyte Studies in Polycythemia Vera Treated with Radiophosphorus. C. F. Stroebel and D. G. Hanlon. Minnesota Med. 42:10-12 (Jan.) 1959 [St. Paul].

The authors studied the leukocytic activity, based on quantitative and differential leukocyte counts in the peripheral blood, in 212 patients with polycythemia vera who were treated with radiophosphorus (P^{32}) at the Mayo Clinic. The results of these studies allowed classification of polycythemia vera into 4 subdivisions, namely, simple polycythemia vera (in 68 patients), occult leukocytic polycythemia vera (in 69), gross leukocytic polycythemia vera (in 50), and leukemoid polycythemia vera (in 25). In the patients with simple polycythemia vera, the absolute leukocyte count (determined by multiplying the white blood cell count per cubic centimeter by the total blood volume per kilogram of body weight) was 10 or less circulating leukocytes per kilogram. Myeloid immaturity in the peripheral blood did not exceed 1%. In the patients with occult leukocytic polycythemia vera, the absolute leukocyte count exceeded 10 circulating leukocytes per kilogram, but the relative leukocyte count did not exceed 15,000 leukocytes per cubic millimeter. Myeloid immaturity in the peripheral blood did not exceed 1%. In the patients with gross leukocytic polycythemia vera, the relative leukocyte count was 15,000 leukocytes per cubic millimeter or more, but myeloid immaturity in the peripheral blood did not exceed 1%. In the patients with leukemoid polycythemia vera, myeloid immaturity was noted in the peripheral blood in excess of 1% of the differential leukocyte count. Leukocytosis was or was not present.

This fourfold classification was applied to the study of the remissions occurring in these patients as a result of treatment with P^{32}. The rate of failure of treatment was the same for both groups of patients with simple and occult leukocytic polycythemia vera, but the incidence of long remissions was much higher in the patients with simple polycythemia vera. The over-all picture of resulting status also showed a definite relation to the leukocytic types: the condition of 58 (85%) of the 68 patients with simple polycythemia vera remained relatively simple; that of 43 (62%) of the 69 patients who had initially the occult leukocytic type of the disease became and remained relatively simple, while the conditions of only 22 (42%) of the 50 patients with gross leukocytic polycythemia vera and of 7 (28%) of the 25 patients with the leukemoid type of the disease became and remained relatively simple in type. These findings showed that the fourfold classification of polycythemia vera is of some prognostic importance. When granulocytic hyperplasia is present, the incidence of therapeutic failure is higher, more P^{32} is needed for control, and the greater is the chance for the development of either a leukemoid state or an acute leukemia.

Massive Intraperitoneal Hemorrhage Due to Paracentesis. N. Hakim, W. Hasbrouck and R. K. Spiro. J. M. Soc. New Jersey 56:19-21 (Jan.) 1959 [Trenton].

The authors present the history of a 65-year-old woman who on admission gave the impression of (1) having rheumatic heart disease with auricular fibrillation, mitral stenosis, and insufficiency, (2) congestive heart failure, and (3) likelihood of digitalis intoxication and pelvic pathology. A diagnostic abdominal tap was made to determine the nature of the ascitic fluid. A no. 18 gauge needle was introduced into the left lower quadrant at a point 5 cm. below the umbilicus in the anterior axillary line. This was the only area free of operative scars and palpable organs. No fluid was obtained on penetration of the peritoneal space. Bleeding at the site of the skin puncture was greater than normally encountered, but it was easily stopped. One hour after this procedure the patient appeared to be apprehensive. Her skin was pale, cold, and clammy. The degree of abdominal distention was unchanged. The only new finding was tenderness at the site of paracentesis. Possible perforation of an aberrant blood vessel or spleen was suspected.

Forty-eight hours after paracentesis the abdomen was very tense, and an exploratory laparotomy was decided upon. Approximately 6 liters of hemoascitic fluid was aspirated from the peritoneal cavity. A large accumulation of blood clots (limited chiefly to the pouch of Douglas and the area of the previous uterine suspension) was also removed. Beneath the site of paracentesis was the area of a firm fibrinous clot, measuring 3 by 6 by 10 cm., which surrounded a dilated omental varix. There was no active bleeding. The postoperative course was uncomplicated. It is believed that the bleeding had stopped 6 to 8 hours after the diagnostic peritoneal tap, as substantiated by the stability of the hematocrit and the level of the hemoglobin after the initial drop. Possible hepatic dysfunction secondary to congestive failure may also have played a role in the hemorrhage. The antihemorrhagic drugs may have helped establish hemostasis. The subsequent symptoms of an acute "surgical abdomen" were probably the result of the intraperitoneal hemorrhage causing peritoneal irritation, increasing abdominal distention, traction on surgical adhesions, and localization of clots in the pelvic floor. It is suggested that the possibility of an intra-abdominal bleeding be considered one of the causes of shock after paracentesis in cases of portal hypertension and ascites.

Toxoplasmosis: Review of Toxoplasmosis in Connection with Report of an Apparently Congenital Case Diagnosed in an Adult. R. K. Westby. Tidsskr. norske lægefor. 78:1238-1240 (Dec. 15) 1958 (In Norwegian) [Oslo].

Toxoplasmosis occurs in both congenital and acquired form. In congenital toxoplasmosis, hydrocephalus is seen in about 80% of the cases and is due to obstruction of the cerebral aqueduct or the interventricular foramen on both sides. There are intracranial calcifications in about half of the cases. Chorioretinitis, found in 60 to 70% of cases, is usually central and bilateral; in an early stage it is exudative and proliferative, but it later passes into an atrophic stage. Depending on the extent of the pathanatomic changes in the cerebrum, a number of neurological changes occur. Generalized or local convulsions occur in 60 to 70% of the cases. There is almost always mental reduction, varying from the lightest to the severest degrees. Sometimes Toxoplasma organisms are demonstrable in the spinal fluid. Some patients die soon after birth, many have grave defects due to brain and eye injury, others have relatively few symptoms. Acquired toxoplasmosis may present an acute generalized form, acute or subacute meningo-encephalitis, febrile or afebrile lymphadenitis, and monosymptomatic and asymptomatic forms. In a man, aged 60 years, with diagnosis of congenital toxoplasmosis based on the clinical findings, there were hydrocephalus, intracranial calcifications, chorioretinitis, history of generalized convulsions soon after birth, and positive dye test. The dye test was positive in a low titer, which was to be expected so many years after active infection.

SURGERY

Recurrent Mitral Stenosis: An Increasingly Common Occurrence Due to Inadequate Mobilization of the Valve. C. P. Bailey and D. P. Morse. J. Internat. Coll. Surgeons 31:8-23 (Jan.) 1959 [Chicago].

Of 1,607 patients with mitral stenosis who underwent mitral commissurotomy by the older left-sided approach, there was recurrence of the disease in 44, as was proved either at reoperation or at autopsy. It appeared that the early operations performed on these patients enlarged the mitral orifice enough to give relief of symptoms, but this was not usually enough for objective evidence of relief of the obstruction as evidenced by a change in the size of the heart or disappearance of the diastolic murmur. Gradual reclosure of these scarred valves may take place over a period of years (averaging over 4 years in this series) without a recurrent attack of rheumatic fever.

It is now possible routinely to perform an operation for mitral stenosis that effectively returns the valve to a normal functional capacity. The new operation, for which the term "neostrophingic mobilization of the septal leaflet" has been coined, and which usually can be performed only by the right-sided thoracic approach, entails opening of both commissures to their full curving extent and well into normal flexible valve tissue, so that the new septal leaflet is freely hinged at its base. In addition, it is essential to establish complete bipolar separation of the cross-fused subvalvular chordopapillary structures. The usual size of the valve observed at operation is 1 sq. cm. or less. The average orificial size provided by the older left-sided approach, as determined by catheterization, was less than 2.5 sq. cm. By the new procedure one can obtain a valve area ranging from 4 to 6 sq. cm. in 80% of the patients, thus producing objective as well as subjective evidence of relief of the obstruction. In 50% of the patients the diastolic murmur has been abolished.

Cardiac Ventriculography in the Selection of Patients for Mitral Valve Surgery. J. F. Uricchio, J. S. Lehman, W. M. Lemmon and others. Am. J. Cardiol. 3:22-27 (Jan.) 1959 [New York].

In selecting patients for mitral commissurotomy, the authors employed cardiac ventriculography-left (a roentgenologic technique consisting of opacification of the left ventricle by direct transthoracic needle puncture) in 42 patients with isolated rheumatic disease of the mitral valve. Of these 42 patients, 28 with significant mitral regurgitation, proved at surgical intervention, had a significant degree of reflux opacification of the left atrium (varying from 2+ to 4+). Of the remaining 14 patients with significant mitral stenosis, proved at surgery, 9 did not have any reflux opacification of the left atrium, while the other 5 patients showed a slight degree of reflux opacification (1+). No deaths occurred among the 42 patients, and there was no appreciable morbidity in this group, although serious complications may occur if the test is not performed with care. The chief indication for cardiac ventriculography-left appears to be present in those patients in whom there is uncertainty as to the presence or absence of major mitral regurgitation and the exact degree of stenosis. Preoperative estimation of such regurgitation is important, because mitral commissurotomy without correction of the regurgitation will not benefit the patient.

Leuko-Erythroblastic Anaemia in Breast Cancer Treated by Hypophysectomy. H. Hortling, K. Malmio, G. A. Björkesten and L. Hiisi-Brummer. Acta med. scandinav. 162:387-396 (no. 5) 1958 (In English) [Stockholm].

The authors studied 42 patients with metastatic cancer of the breast, on whom hypophysectomy was performed because any other form of treatment hitherto used was refractory. In 8 of the patients leukoerythroblastic anemia was observed before the operation; in 7 of these the effect of the hypophysectomy could be evaluated, and they were followed up from 19 months to 5 years. Diagnosis of leukoerythroblastic anemia was established when the presence of normoblasts or macroblasts or an increased number of granulocytes, i. e., myelocytes or metamyelocytes, could be identified in the peripheral blood. In one patient the only hematological symptom was an increase in rod-like nuclear granuloblasts to an average of 10%. In 7 patients on whom sternal puncture was performed, cancer cells were found. Ordinary routine methods did not reveal any clear signs of hemolysis in any of the patients. The blood picture returned to normal after hypophysectomy in 3 of the 7 patients, whereas an obvious remission of the hematological abnormalities was observed in another 3; in 1 patient improvement of the blood picture resulted, but apparently the disease affected the liver and the patient died.

The effect of hypophysectomy was dramatic in an apparently hopeless situation in one patient whose history is described in detail. A 52-year-old woman experienced pain in the back as a first symptom of cancer of the breast. In September, 1955, a radical operation, with removal of the axillary lymph nodes, was performed. In October metastases were detected in 3 vertebrae; in addition, anemia was observed. Roentgen-ray treatment was given to the vertebrae, and roentgenologic castration of the ovaries was performed. A tendency toward anemia and leukopenia developed. Androgenic therapy was administered for 8 months. The blood values became normal in March, 1956, but in August a rapid aggravation of the general condition and a deterioration in the blood picture occurred. Cortisone was given for 3 weeks, and hypophysectomy was performed in September. Five weeks after the operation an obvious improvement began, and the patient was practically free of symptoms until April, 1958, when a progressive leukoerythroblastic anemia developed again and death occurred in August. The authors' observations suggest that in cases of mammary cancer metastases in the bone marrow, with resultant leukoerythroblastic anemia, a remission may be attained by hypophysectomy when other types of treatment, including endocrine therapy, have failed.

Contribution to Reoperations on the Bile System (Causes, Indications, Results). B. Kourias, A. Sapkas and C. Athanassakos. Chirurg 30:1-10 (Jan.) 1959 (In German) [Berlin].

Of 1,432 patients with cholecystitis, who were operated on in the surgical clinic of the Greek Red Cross Hospital in Athens and in other hospitals in Greece between 1945 and 1958, 922 had a cholecystectomy performed, 384 underwent cholecystectomy and drainage of the common bile duct, 36 had an anastomosis between the common bile duct and the duodenum, 65 underwent cholecystostomy, and 25 had miscellaneous operations. Thirty-six (2.51%) of the 1,432 patients had to be subjected to reoperation for serious postoperative conditions from 40 days to 12 years after the first operation. Of these 36 patients, 22 (61%) had had their first operations performed at the Greek Red Cross Hospital in Athens, and 14 (39%) had been operated on in other hospitals in Greece.

The patients were subdivided into 9 groups according to the pathological condition which made reoperation necessary. The first group consisted of 22 patients (63%) in whom stones had remained in the common bile duct; 8 of these had undergone a cholecystectomy as the original operation, and 14 had had a choledochotomy. Considering the total number of 1,432 patients operated on, stones had remained in 1.1% of those who had undergone cholecystectomy and in 3% of those who had undergone choledochotomy. In half of these patients the stones were located in the hepatic or intrahepatic ducts. Omission of careful exploration of the common bile duct for stones, omission of cholangiography or manometry, the presence of a pseudodiverticulum or pouch of the common bile duct, lithiasis of the hepatic and intrahepatic ducts, early interruption of the original operation because of the patient's reduced tolerance, and congenital anomalies of the hepatic and bile ducts were found to be the causes for the postoperative remaining of stones.

Regarding the other groups, the second consisted of 2 patients with functional disturbances of the sphincter of Oddi; the third consisted of 2 patients with a cicatricial stricture of the ampulla of Vater; the fourth consisted of 2 patients with chronic pancreatitis; and the fifth consisted of 3 patients with traumatic or phlegmonous stricture of the hepatic and common bile ducts. Groups 6, 7, and 8 consisted of one patient each, with disturbances caused, respectively, by leaving the stump of the cystic duct too long, aneurysm of the hepatic artery, and a hydatid (echinococcus) cyst in the liver. The 9th and last group consisted of 2 patients who underwent exploratory operations for erroneously suspected stones.

Reoperation consisted of choledochotomy combined with removal of stones and drainage, choledochoduodenostomy, dilatation of the ampulla of Vater, sphincterotomy, removal of newly formed gallbladder, hepaticojejunostomy, transjejunal dilatation of a previously performed hepaticojejunostomy, removal of an echinococcus cyst, and exploratory laparotomy. There were 3 operative deaths (an operative mortality rate of 8.5%), and 2 patients died later. Of the 31 surviving patients, 30 (more than 90%) were in excellent health 6 months to 13 years after reoperation, and 1 was lost to follow-up. All the reoperations were performed with the aid of cholangiography and occasionally with manometric control.

Pancreatico-Gastrostomy in Pancreatico-Duodenal Resection for Carcinoma of the Head of the Pancreas or the Papilla of Vater. E. Millbourn. Acta chir. scandinav. 116:12-27 (no. 1) 1958 (In English) [Stockholm].

The author performed pancreaticogastrostomy on 7 patients for a malignant tumor of the head of the pancreas or the region of the papilla of Vater. The operations were performed in the department of surgery of the Centrallasarettet in Kalmar, Sweden, in 1947 and 1948. After pancreaticoduodenal resection, the distal end of the stomach was opened through a transverse incision made in its posterior wall, and the stump of the pancreas was brought into the stomach with the aid of long mattress, "stay" sutures. The whole cut surface of the pancreatic end was then secured with interrupted silk sutures into the stomach, through the incision in the posterior wall. The first row of sutures was made from the inside and the second from the outside of the stomach. When possible, omentum was fixed around the pancreaticogastrostomy. A large rubber drain, with side-openings and containing a smaller rubber tube for intermittent suction, was placed in the bottom of the operation area through a stab wound below the right costal margin, proximal and distal to the pancreaticogastrostomy, although not in direct contact with the suture line. In none of the 7 patients did pancreatic, jejunal, or gastric juice or bile ever occur in the fluid drained. The drain permitted early ambulation. Good healing without leakage or fistula formation in the pancreaticogastrostomy resulted in all the patients.

Pancreaticogastrostomy is somewhat easier to perform than pancreaticojejunostomy. Pancreaticogastrostomy permits repeated studies, even during a long postoperative course, of the excretory function of the pancreas and at the same time of the patency of the stoma. If amylase and trypsin activity is shown in the gastric juice (saliva being always removed by suction during the amylase determinations), the stoma must be patent if no aberrant pancreatic tissue is present in the stomach or in the nearest portion of the jejunum. Trypsin determinations give more reliable information than amylase determinations. In all 7 patients, the surgical intervention created a patent anastomosis for varying periods. In 3 patients, who survived the radical operation for periods varying from 9 months to 2 years and 7 months, the patency of the anastomosis was revealed at autopsy, and in 2 other patients the patency was revealed by trypsin determinations of the gastric juice 2¼ and 3½ years, respectively, after the surgical intervention. The anastomosis thus remained patent for several years even though the pancreatic duct was small at the surgical intervention. Postoperative obliteration occurred about 2 years after radical surgical intervention in one patient. Reoperation with a new pancreaticogastrostomy (side-to-side) was successfully performed 2 years and 9 months after radical resection.

In none of the 7 patients did the flow of the pancreatic juice into the stomach give rise to subjective discomfort. They did not complain of dyspepsia, and the stools were normal so long as the pancreaticogastrostomy was patent. Postoperative examination of the gastric juice showed achlorhydria in the 6 patients who most recently underwent pancreaticogastrostomy. This postoperative achlorhydria probably was the result of pancreatic juice emptying into the stomach, and it is to be considered an important factor in the avoidance of ulcer formation in the gastrojejunal stoma. Pancreaticogastrostomy is recommended in radical pancreatic resection instead of pancreaticojejunostomy, despite the limited number of patients reported on.

Rapid Relaxation of the Right Atrium in the Treatment of Cardiac Arrest Occurring in the Course of Surgical Operation. F. Morino and R. Gentilli. Minerva chir. 13:1309-1320 (Nov. 30) 1958 (In Italian) [Turin, Italy].

The authors report on 2 patients who suffered cardiac arrest during the course of a surgical operation. The heart was reactivated in both patients by causing a rapid relaxation of the right atrium. In the first patient, an 8-year-old child, arrest of the heart occurred while an attempt was being made to isolate the aorta. No result was obtained by injecting epinephrine and massaging the heart for about 10 minutes. Inasmuch as a marked distention was noticed in the walls of the myocardium, a syringe with a large needle was introduced into the right atrium, and the distention was relieved momentarily by extracting rapidly 50 cc. of blood. Massaging the heart was then started at once, and after a few rhythmic compressions the heart started pulsating spontaneously. After 15 minutes of rest the operation was continued and was completed without further incident. In the second patient arrest of the heart occurred in the course of opening the pericardium. The heart beat was restored after extracting 50 cc. of blood from the right atrium and massaging the heart. The operation was continued after a 20-minute rest and was completed with no further complications.

Sarcoma of the Stomach. B. Thorbjarnarson, J. M. Pearce and J. M. Beal. Am. J. Surg. 97:36-42 (Jan.) 1959 [New York].

The authors report on 50 patients, between the ages of 16 and 79 years, with sarcoma of the stomach who were treated on the pavillion service of the New York Hospital between 1932 and 1958. Of the 50 patients, 37 had lymphoma, 11 had leiomyosarcoma, 1 had myxosarcoma, and 1 had fibrosarcoma. During the same period, 670 patients with malignant neoplasms of the stomach were observed, so that sarcoma represented 7.4% of all malignant lesions of the stomach. Pain, weight loss, and bleeding were, in order of frequency, the most common symptoms. The clinical and laboratory findings seldom led to the correct diagnosis before surgical intervention. Thirty-two of the 37 patients with malignant lymphoma of the stomach were subjected to definitive surgical removal of the neoplasm. There were 2 deaths after the surgical intervention, representing an operative mortality rate of 5.4%. Thirteen patients survived for 5 years or longer. Since 28 of the 37 patients were admitted to the hospital before 1953 and 24 of these were subjected to definitive surgical removal of the neoplasm, the 13 patients represented 59% of those who were eligible for computation of 5-year survival rates.

Of the 13 patients with other sarcomas than lymphoma of the stomach, 12 were subjected to surgical intervention. There was one postoperative death. Six patients survived for more than 5 years; one died of recurrence 6 years after the operation. Thus, of the entire group of 50 patients, 19 patients survived for 5 years or longer. The prognosis for patients with sarcoma, therefore, is considerably better than for those with carcinoma. Roentgenotherapy is recommended for patients with lymphoma of the stomach but not for patients with other types of sarcoma of the stomach.

Strangulated Femoral Hernia: A Review of 170 Cases. F. A. Rogers. Ann. Surg. 149:9-20 (Jan.) 1959 [Philadelphia].

A femoral hernia is more likely to undergo acute incarceration and subsequent strangulation than any other common hernia. Strangulation constitutes an urgent surgical emergency. Acute incarceration occurs more frequently in this type of hernia because the small femoral ring, through which the herniation occurs, is more rigid and because herniation through the defect occurs in a more vertical or downward direction. It is this latter factor, uniquely characteristic of the femoral canal hernia, which contributes to the difficulty in reducing it. This study on acutely incarcerated and strangulated femoral hernia was undertaken primarily to discover the results of treatment.

The data from clinical charts of 170 patients treated over a 15-year period on the College of Medical Evangelists surgical service at the Los Angeles County Hospital were tabulated by I.B.M. machine. The group included 116 women and 54 men, 71% of whom were in the age decades of 60 to 90 years. Eight of the 105 patients who knew that they had a hernia had had previous incarcerations. Most of the 12 deaths in this group could have been prevented by elective repair of the hernia. The diagnosis of hernia was made for the first time in 61 of the patients. Vomiting is a prominent symptom. A mass in the femoral region is the most important single physical finding. Acute strangulation of a femoral hernia is a common cause of acute intestinal obstruction among patients more than 50 years of age. When intestinal colic associated with vomiting suggests acute intestinal obstruction, hernial orifices should be carefully examined for the presence of a mass. A femoral hernia and an incarcerated inguinal hernia can be differentiated. The femoral hernia is palpable below and lateral to the pubic spine, while the inguinal hernia is found to lie superiorly and medially to the pubic spine.

In the series reported, when the correct diagnosis was made early, the over-all mortality was low. When the patients had been admitted to hospital services other than general surgery and the proper diagnosis was delayed, the mortality reached 50%. The incidence of gangrene rose sharply as the delay in diagnosis increased. Delay in surgery for any reason greatly increased the number of deaths. Many patients reached the hospital in shock. Others had suffered fluid and electrolyte loss and required replacement therapy before operation could be carried out. An adequate surgical approach is important, and the excellence of the Cheatle-Henry extraperitoneal, retropubic operation is emphasized. The over-all mortality rate for this series was 13%. The male operative mortality was 20%, while that of female patients was only 10%. Thirty-five patients required resections of gangrenous portions of the small intestine; there were 9 deaths in this group. Postoperative complications occurred in 37 patients, and there was a 6.6% wound infection rate. An elective repair of all femoral hernias is advisable.

The Value of Intra-Articular Injections in Osteoarthritis of the Knee. J. H. Miller, J. White and T. H. Norton. J. Bone & Joint Surg. 40B:636-643 (Nov.) 1958 [London].

The authors report on 59 men and 122 women with osteoarthritis of the knee treated by intra-articular injections. The 181 patients were accepted for treatment, provided that pain was present when treatment was begun and was not showing any tendency to subside, that positive roentgenologic evidence of osteoarthritis was present, and that treatment had not been given previously. Three solutions, chosen as typical of those in common use, were employed for injections, namely, lactic acid solution, procaine (Novocain) hydrochloride solution, and hydrocortisone solution. Isotonic sodium chloride solution and mock injection (given with a special syringe, with which neither air nor fluid could be injected into the joint, although the same visual effect was produced by this device as by fluid) were used for control purposes. Each patient was allotted 1 of the 5 types of injection at random, and the same type of injection was used throughout his or her treatment, which consisted of 5 injections at intervals of 2 weeks. Each patient was reviewed on 2 occasions, 6 weeks and 6 months after the end of the treatment.

Irrespective of the type of injection used, including the controls, no significant difference in the effects was demonstrated in the results. From the point of view of the assessing physician, there was found an appreciable objective improvement, which was fairly evenly distributed. Presumably, this indicates a more natural and confident use of the joint, and is a reflection of the change in outlook of the patient after the injections. The objective assessment also showed that the percentage of improvement was higher among men than among women. Between the men and the assessor agreement was almost complete, but more women expressed satisfaction than the assessor was prepared to accept on clinical grounds. The inference is that women are more susceptible to suggestion in this form of treatment, and here again the psychological element must be taken into account.

Most patients in each group expressed satisfaction with their treatment. This does not depend at all on the injection of any particular substance into the joint, but rather on the psychological atmosphere created. The use of joint puncture can, therefore, be accepted as a reasonable placebo in the care of osteoarthritis. It follows that, if puncture is decided upon, the least noxious and most economical substance (isotonic sodium chloride solution) or none at all (mock injection) should be used.

The Environmental Distribution of Staphylococcus Aureus in an Operating Suite. R. I. Wise, F. J. Sweeney, G. J. Haupt and M. A. Waddell. Ann. Surg. 149:30-42 (Jan.) 1959 [Philadelphia].

At the Jefferson Medical College Hospital in Philadelphia an attempt was made to determine the presence and extent of contamination by staphylococci in the operating rooms and to detect the source and mode of entry of the pathogenic bacteria into clean surgical wounds. All the material for bacteriological investigation was collected during 71 operative procedures. A total of 1,096 cultures were obtained in 5 days. This number included 206 nasal cultures, which were obtained by moistening swabs with nutrient broth and introducing a swab into the anterior nares of every person entering the operating rooms. It was found that members of the hospital staff who had close contact with infected patients had a greater incidence of coagulase-positive cultures of staphylococci isolated from the anterior nares. Many different bacteriophage types of Staphylococcus organisms were detected in the anterior nares of the 136 persons who entered the operating rooms during the 5 days from Aug. 13 to Aug. 17, 1956. Five of these types were known to cause postoperative wound infections during the period from July 1 to Oct. 31, 1956, and were isolated from 13% of the personnel. Other strains were isolated which were not implicated in any infection during the period.

Staphylococci were isolated from the interior of 90% of 481 surgical gloves at the conclusion of the surgical procedures. The mean bacterial count was 4,212 per glove. Coagulase-positive staphylococci were isolated from 14% of the gloves, but none of the strains from gloves was susceptible to bacteriophage. Approximately 10% of the surgical gloves were punctured or torn during surgery. Coagulase-positive staphylococci were isolated from 11% of samples of skin obtained from the edge of incisions, from 8% of samples of solution used in rinsing instruments during surgery, and from 17% of surgical incisions which were cultured just prior to closure. These strains, with 2 exceptions, were not typeable with bacteriophage. Various fomites, such as talcum powder, rubber drains, tubes, soaps, brushes, and surgical packs, were found to have a low incidence of viable bacteria. The air of the operating rooms contained chiefly staphylococci but mixed with other bacteria. The contamination of the air became greater as the number of persons in the room increased. None of the cultures of coagulase-positive staphylococci obtained from the air was typeable with bacteriophage.

Infections of deep surgical wounds developed in 2 of the 71 patients in this series. In both instances coagulase-positive staphylococci were isolated from the infectious processes, but the cultures were not typeable with bacteriophage, and so it was not possible to trace the source of these infections. The authors stress the need for rigid aseptic techniques to prevent hospital personnel from becoming carriers of pathogenic bacteria and from spreading these bacteria to susceptible hosts. The prophylactic use of antibiotics cannot be substituted for aseptic techniques, since the strains causing the infections are usually resistant to the action of the commonly used antibiotics.

The Management of Pathological Fracture of the Major Long Bones from Metastatic Cancer. R. A. Bremner and A. M. Jelliffe. J. Bone & Joint Surg. 40B:652-659 (Nov.) 1958 [London].

The authors report on 40 patients (29 women and 11 men) with disseminated cancer. Thirty-three of these patients had 36 pathological fractures of the long bones (double fractures having been sustained by 3 patients), for which they were treated by internal fixation and irradiation, and 7 patients received the same treatment for "prophylactic" reasons, since they had destructive lesions of the long bones from metastatic cancer. Nineteen of the 40 patients had cancer of the breast; 8 had bronchial carcinoma; 13 had carcinoma of the thyroid, carcinoma of the rectum, epithelioma of the scalp, malignant angioendothelioma of the nasopharynx, carcinoma of the kidney, carcinoma of the esophagus, and multiple myelomatosis, respectively; and in 3 the site of the primary tumor was undiscovered. Of the 43 lesions, the neck and trochanteric region of the femur was involved in 19, the upper third of the shaft of the femur in 10, the middle third of the shaft of the femur in 8, and the humerus in 6.

All the patients were treated by internal fixation at the earliest opportunity, either by an intramedullary nail or in the case of some lesions near the subtrochanteric region, where an adequate grip could be obtained for plate screws below the lesion, by a nail and plate. All were also given irradiation therapy, and, when intramedullary fixation had been employed, the whole length of the involved bone was irradiated. Excluding the patients treated "prophylactically," 25 (83%) of the 30 patients who had sustained a fracture of the lower extremity survived for more than 6 weeks, and all returned to walking with crutches; union occurred in 80% of these fractures. Four of the 5 patients who had sustained a fracture of the humerus survived to regain a functionally useful arm, and 3 of the fractures united. "Prophylactic" internal fixation and irradiation therapy appeared to be helpful in 5 of the 7 patients.

The danger of disseminating tumor cells, either generally or locally, is the main criticism of this method of treatment. In those patients in whom irradiation therapy was used to cover the whole of the operation area, there was no evidence of spread into the soft tissues locally or along the medullary canal. Internal fixation might not be justified in the treatment of a single metastasis from a primary tumor of low-grade malignancy carrying a prognosis of several years, but, in general, the theoretical dangers of dissemination may be ignored. The difficulties of the technique are easily surmountable and have probably been overemphasized in the past. Internal-fixation and irradiation therapy is the best method at present available for dealing with the difficult problem of management of a pathological fracture of a major long bone through a metastatic cancer deposit.

Some Comments on the Treatment of Fractures of Long Bones in Children (With Special Reference to 3,594 Cases). J. Desbrosses, J. Rebouillat, C. Bosser and M. Guilleminet. Presse méd. 66:1929-1930 (Dec. 6) 1958 (In French) [Paris].

Conclusions are drawn from a large collection of statistics gathered from 3,594 cases on the infants' surgery service of Debrousse Hospital and at the orthopedic and infant surgery clinic of Edouard Herriot Hospital in Lyons. The authors have sought to show the respective parts that manual reduction and surgical methods play in fractures of the long bones in children from 1 to 15 years old. They particularly noted the predominant incidence of location of fractures in the upper extremity, fractures being located in this extremity in 2,742 out of 3,594 cases (or 70.2%). The upper extremity was chiefly affected at the level of the forearm (1,364 cases) and at the elbow (797 cases). In the latter case, surgical reduction was often required, not essentially for reasons of the immediate subsequent vasculonervous complications but on account of the functional future, which might be heavily compromised by a defective bone alignment, an antibrachial abutment, or a stiffened joint. All juxta-articular or articular fractures in the child should be carefully reduced to avoid severe hazards. Out of 126 cases of external condyle fracture, 32 were surgically reduced, or 25%, which is one of the highest operative percentages. Conservative management should be tried, but this occasionally proves inadequate, especially for the elbow, which in this study required operation in 18.3% of the cases.

According to the authors' findings, fractures are much less frequent in the lower extremity and are much less operable. The femoral diaphysis is the bone which is most often operated on. In this series, 11% of the fractures of this type were operated on (40 interventions out of 364 fractures), but this was an unusually large number owing to the particular circumstances. All fractures of the ends of the tibia were treated orthopedically, and only 24 fractures of the tibial diaphysis, out of 443 such fractures, had to be osteosynthesized. This study shows the authors' tendency first toward utilizing manual reduction of fractures and then toward having recourse to surgery in carefully chosen cases when it alone can have satisfying results. There was surgical reduction in 22.2% of the fractures of the upper extremity and in 7.7% of the fractures of the lower extremity in this series. The over-all percentage of fractures which were operated on was only 9.4% (340 out of 3,594 fractures).

Diverticula of the Duodenum (Contribution of Cases and Clinical Considerations). A. Jovine and G. Francini. Acta chir. ital. 14:743-771 (Sept.-Oct.) 1958 (In Italian) [Padua, Italy].

Nine patients with duodenal diverticula, observed at the surgical clinic of the University of Padua in the last 12 years, are reported on. Comparison of the data available from these patients and those available in the literature shows that duodenal diverticula are frequent but that most of the time they are asymptomatic. Only in a small number of cases have duodenal diverticula caused such disturbances as to make surgical intervention necessary. Roentgenologic examination was found very useful by the authors in studying the diverticular formations and the various other organs in which concomitant lesions could be present. Medical therapy is indicated unless surgical intervention is made necessary by major complications. Whether resection or invagination of the diverticulum must be performed is to be decided by taking into consideration the state of each patient. Palliative interventions, such as gastroenteroanastomosis, are indicated when resection or invagination may be too dangerous.

NEUROLOGY & PSYCHIATRY

Dystonia Musculorum Deformans Alleviated by Chemopallidectomy and Chemopallidothalamectomy. I. S. Cooper. A. M. A. Arch. Neurol. & Psychiat. 81:5-19 (Jan.) 1959 [Chicago].

The author reports on 16 children with advanced dystonia musculorum deformans, which has previously been demonstrated to be a progressive incapacitating disease of childhood, characterized by involuntary movements and deformities of the entire body. This disease has heretofore been considered to be unresponsive to medical, surgical, physical, or psychiatric therapy. The author subjected the patients to chemopallidectomy and/or chemopallidothalamectomy; in these operations well-localized but sufficient-sized lesions were accurately placed in the globus pallidus and/or ventrolateral nucleus of the thalamus. In 3 patients the operation was performed bilaterally. Thirteen of the 16 patients obtained marked alleviation of the involuntary movements and deformities of this previously intractable, progressive disease. The cases of 5 of the 13 patients, 2 boys, aged 16 and 18 years, and 3 girls, aged 12, 10, and 13 years, respectively, are reported on in detail, illustrating this alleviation. Such relief has now persisted for more than 2 years in several of these patients. The entity of dystonia musculorum deformans can no longer be considered as a hopeless, irreversible disease. Chemopallidectomy and/or chemopallidothalamectomy is the treatment of choice in alleviating it.

Therapeutic Possibilities During the Acute Stage of Heine-Medin's Disease (Poliomyelitis). H. Zischinsky. München. med. Wchnschr. 101:30-33 (Jan. 2) 1959 (In German) [Munich, Germany].

The author shows that an effective specific therapy is not available for acute anterior poliomyelitis. Treatment with serum of convalescents, with gamma globulin, or with antibiotics all proved ineffective. In view of the pathogenesis of poliomyelitis, an effective specific treatment is even theoretically impossible. Laboratory studies on a patient, whose history is presented, indicate that *viremia and invasion of the virus into the central* nervous system take place at a time when there is as yet no suspicion of poliomyelitis. For this reason therapy will always come too late, even if a specific therapy were available. Much can be done during the acute stage of poliomyelitis. Good nursing care is important. Paralysis of deglutition and respiration demands special measures. These are most effectively supplied in special poliomyelitis centers staffed with suitably trained teams and equipped with all instruments and devices for therapy and rehabilitation.

The Use of Ritalin in Psychotherapy of Depressions of the Aged. A. Jacobson. Psychiat. Quart. 32:474-483 (July) 1958 [Utica, N. Y.].

The author investigated the effectiveness of methylphenidate (Ritalin) hydrochloride, a new central nervous system stimulant and antidepressant, in facilitating psychotherapy in depressed patients of the involutional age group. Patients, including both those with reactive and those with involutional depressions, undergoing psychotherapy and simultaneously receiving Ritalin, were evaluated regarding changes in alertness, sense of well-being, dissipation of morning fatigue, cooperativeness in psychotherapy, and ability to function socially and otherwise. A placebo was substituted for Ritalin in a second comparable group of patients. Each group included 27 patients; all were in the 6th and 7th decades of life. Patients recognized as manic-depressive were excluded. Ritalin was given in doses ranging from 10 to 30 mg. 3 times in the first 8 hours of the day, at spaced intervals. All the patients were ambulatory and were considered fair-to-good subjects for extramural care, inasmuch as suicide was not believed an imminent threat.

The author's chief aim was effective psychotherapy, which is difficult in depressed patients because, by the very nature of their illness, they have difficulty in sharing their thoughts and feelings with others. It was his impression that Ritalin had a place in opening this communication barrier to effective psychotherapy. The drug facilitated communication and cooperation chiefly by its mood-elevating effects. The psychomotor stimulation was without significant effect on the blood pressure; furthermore, there was no depressive let-down as the effects of the drug wore off. Twenty-two of the 27 patients receiving Ritalin showed slight to marked improvement. Five patients showed no improvement and required hospitalization and/or electric convulsive therapy. Of the group of 27 patients who did receive a placebo instead of Ritalin, 11 showed minimal to moderate improvement; 16 required hospitalization and/or electric convulsive therapy. Four illustrative case histories are presented.

Ritalin appeared to increase the effectiveness of psychotherapy with elderly depressed patients. As *in an earlier paper, the author was impressed* by the increase in alertness, and the dissipation of early morning depression and fatigue and by the lack of evidence of addiction. The usefulness of Ritalin in counteracting the lethargy or oversedation of ataractic drugs was also mentioned.

Human Infection with Listeria Monocytogenes: Review of Main Features of Listeriosis. O. Jessen. Ugesk læger 120:1701-1707 (Dec. 18) 1958 (In Danish) [Copenhagen].

Human infection with Listeria monocytogenes is regarded as rare in Denmark, but the number of cases reported is thought not to reflect the true frequency. Both human and animal listeriosis is spread over the entire globe. The reaction of the organism to the bacteria is typical: there is either supuration, with a considerable number of mononuclear cells in the pus, or formation of miliary granulomas (listeriomas), with a central coagulation necrosis and peripheral accumulation of reticuloendothelial cells, leukocytes, and monocytes. The symptoms occur in different combinations, with transition forms. The 2 most important syndromes are presumably meningoencephalitis and the septic granulomatous form in infants. Clinically, meningitis due to L. monocytogenes is not distinguishable from other forms of bacterial meningitis. It may be preceded by a short prodromal stage. The further course is marked by meningeal and cerebral symptoms. The course is often violent; it may be subacute. In some cases the disease passes into a subchronic stage, with persistence of bacteria in the spinal fluid for months, and is clinically marked by neuropsychiatric symptoms and moderate fever. The peripheral picture is marked by neutrophil granulocytosis. Disseminated granulomatosis in infants (granulomatosis infantiseptica) is transmitted from mother to child in utero, perhaps now and then to the child during birth. In most cases of pregnancy listeriosis, a retrospective diagnosis is not possible. With signs of grave disease in the newborn infant, listeriosis should be considered. During the course of a localized infection, hematogenic spread may cause metastatic foci in practically every organ.

Early and adequate antibiotic and chemotherapeutic treatment has decisively improved the prognosis in listeriosis. The treatment must be continued for at least 10 days after disappearance of clinical symptoms. Excellent results have been attained with the tetrayclines. Treatment with penicillin, together with sulfonamides, has been effective in some cases, but seems less reliable. In the American literature erthromycin is recommended, especially combined with penicillin.

Dissecting Aneurysms of the Carotid Artery Following Arteriography. J. F. R. Fleming and A. M. Park. Neurology 9:1-6 (Jan.) 1959 [Minneapolis].

The authors report on a 58-year-old man and on a 32-year-old woman in whom a dissecting aneurysm of the common carotid artery occurred in the wall of the artery as a complication of percutaneous carotid arteriography at the site of needle puncture, with narrowing or occlusion of the arterial lumen. Carotid arteriography had been performed for a subarachnoid hemorrhage from a berry aneurysm on the right internal carotid artery in the man, and for a massive intratemporal lesion causing hemiplegia on the left in the woman. Both patients died, and autopsy was performed on both. In the man, the common carotid artery was narrowed sufficiently to provide massive cerebral hemorrhage. In the woman, the hemorrhage was small and was an incidental finding at autopsy. It is surprising how resistant the vessel wall is to the trauma of puncture. However, large autopsy surveys indicate that in a significant percentage of patients subjected to arteriography a small dissecting aneurysm may occur similar to that observed in the woman. Lesions large enough to occlude the lumen, similar to that which occurred in the man, are very rare, but a few have been reported. Nevertheless, even the smallest intimal elevation may become the site of thrombus formation and thus a possible source of emboli. The clinician should be alert to this complication which may explain certain postangiographic symptoms and may elucidate the interpretation of incomplete filling of the carotid artery in some cases. To prevent a dissecting aneurysm, which may be produced at either the puncture site or the site of perforation of the intima of the posterior wall of the artery, a short, beveled, perfectly sharp needle, as small in diameter as feasible, should be used.

PEDIATRICS

Neurological Involvement in Kaposi's Varicelliform Eruption: Clinical and Electroencephalographic Observations and Considerations. E. Cheli and G. B. Cavazzuti. Minerva med. 49:3961-3968 (Oct. 24) 1958 (In Italian) [Turin, Italy].

Neurological involvement was studied in 8 children, 5 to 12 months old, with Kaposi's varicelliform eruption. The eruption had been contracted by each child in the 3rd or 4th month of life. Fever lasted in each case from 6 to 10 days. Neurological involvement was evidenced by clinical symptoms in 3 children, by changes in the cerebrospinal fluid in 3 (by glycorrhachia in 2 and glycorrhachia, cytoorrhachia, and albuminorrhachia in 1), and by electroencephalographic changes in 2. Three of 4 children who showed neurological involvement on electroencephalographic studies showed no clinical symptoms of neurological involvement, and the spinal fluid was found to be normal. Electroencephalographic findings became normal in one week in 2 of these 3 children; some isolated delta waves, at average voltage, were still present after 12 days in the 3rd child. The authors believe that the neurological involvement in patients with Kaposi's varicelliform eruption is a specific expression of a generic ectodermotropism of the herpetic and vaccine virus causing various pathological manifestations, and that its minimal neurological manifestation can be detected only by means of electroencephalographic studies.

Virus Embryopathies. T. Hellbrügge. München. med. Wchnschr. 101:15-20 (Jan. 2) 1959 (In German) [Munich, Germany].

A review of the clinical, experimental, and embryologic knowledge on the virus embryopathies suggests that transplacental transmission of virus is possible at any time during pregnancy. The resulting damage to the fetus depends upon the stage of pregnancy during which the infection took place. During embryogenesis damage occurs to organs and organ systems that are in the developmental phase, and malformations result. These have their sites of predeliction, such as in the epithelial cells of the crystalline lens, in the sensory cells of the inner ear, in the ameloblasts of the dental primordia, and also in the heart and brain, that is, in cell systems characterized by an intensive nucleoprotein metabolism, which apparently provide favorable conditions for the growth of the virus. Damage produced by a virus has a definite phase specificity, for, regardless of the time of virus infection, it begins only during the stage of differentiation, which is connected with an increased cellular metabolism. This explains the involvement of one or several organs.

When infection is caused by viruses that act slowly, such as the rubella virus, the destructive processes continue for a long time, even after birth, whereas in the case of viruses that act with a sudden explosive effect the destructive processes are clearly evident a few days after infection. Virus invasions do not necessarily cause infections. For instance, if infection with rubella virus occurs during the first month of pregnancy, 25% of the infants show embryopathy. With virus infections in succeeding months of pregnancy, the prognosis for the fetus becomes more favorable, and, if they occur during the last months of pregnancy, the pathological changes in the fetus are similar to those that result from postnatal infection. The incubation periods of the most important virus diseases are listed, and it is suggested that women in the early stage of pregnancy should be isolated from children who either have virus diseases or are likely to be in the incubation period. Pregnant women are likely to forget virus infections that occurred very early during pregnancy, but will sometimes recall them, when the date of the last menstruation is fixed or the days of pregnancy are counted on which the intrauterine injury to eye or ear may have occurred.

Osseous Injuries in the Newborn. W. C. Mitchell and M. B. Coventry. Minnesota Med. 42:1-4 (Jan.) 1959 [St. Paul].

The authors report on osseous injuries in newborn infants observed at the Mayo Clinic. Trauma to the skeleton of the newborn infant is of interest to the family physician, obstetrician, and orthopedist. Primiparous mothers with difficult breech deliveries constitute the largest group with which injuries to the bones and epiphyses of newborn infants are associated. Torsion, traction, and digital pressure are the usual mechanisms of injury. The fracture may be induced deliberately to facilitate delivery of the infant. The newborn infant has such unique propensity for the formation of callus and healing of bones that nonunion is almost unknown. Shortening and angulation of even 40 to 50 degrees usually are corrected by subsequent growth. Consequently, masterful neglect may be legitimate therapy in certain osseous injuries occurring in newborn infants. Fractures of the shaft of the femur require active treatment, and Bryant's traction gives excellent results if used properly. The trauma of a difficult delivery may cause epiphysial or subperiosteal hemorrhage presenting clinical symptoms; however, roentgenologic evidence of injury may not be present until proliferative calcification occurs in the hematoma, which may take 5 to 7 days. Such injuries apparently all heal without residual deformity.

Acute Obstruction of Small Intestine Secondary to Hematoma in Children. A. L. Mestel, G. A. Trusler, S. A. Thomson and C. A. F. Moes. A. M. A. Arch. Surg. 78:25-32 (Jan.) 1959 [Chicago].

The authors report on a 9-year-old girl and an 8-year-old boy with acute obstruction of the small intestine secondary to hematoma. Both had a history of abdominal injury, and both had abdominal pain and vomiting. Laparotomy was performed on the girl and revealed a hematoma of the second, third, and fourth parts of the duodenum which was resected. The child recovered after an uneventful postoperative course. The boy had a history of an undiagnosed bleeding disorder, manifested by several prolonged bouts of bleeding due to trauma and minor surgery. On admission, the patient denied any recent trauma, but the next day it was ascertained that he had been struck in the epigastrium by the butt of a rifle while at play. A tube was passed into his stomach and attached to suction. Dextrose, sodium chloride solution, and blood were given intravenously. A gastrointestinal series of roentgenograms disclosed a large filling defect within the distal duodenal cap and second portion of the duodenum. The stomach appeared to be elevated with indentation on the greater curvature; there was an almost complete obstruction present at the duodenojejunal juncture. The patient's condition remained unchanged for 3 days when he began to have tarry stools. Fresh whole blood (1,650 cc.) and fresh frozen plasma (800 cc.) were given over the next 3 days. Coincidental with the passage of tarry stools, the boy was able to take fluids by mouth, and the duodenal tube was removed. Within several days he was on a normal diet. It was postulated that the duodenal hematoma must have evacuated into the intestine.

Of 19 cases of acute obstruction of the small intestine secondary to hematoma in children which were collected from the literature, 13, in 10 boys and 3 girls, between the ages of 7 days and 15 years, have been reviewed. Eleven of these 13 children had a history of abdominal injury, as the authors' patients did. The most constant clinical features are abdominal pain, vomiting, and leukocytosis. Roentgenologic examination confirms the diagnosis. The condition can be treated without surgical intervention by gastric suction and intravenous administration of fluids. If surgery is performed because of erroneous diagnosis or election, evacuation of the hematoma without resection is the preferred treatment.

Exophthalmic Goiter in Children. A. B. Hayles, R. L. J. Kennedy, O. H. Beahrs and L. B. Woolner. J. Clin Endocrinol. 19:138-151 (Jan.) 1959 [Springfield, Ill.].

There has been considerable controversy as to whether children with exophthalmic goiter are best treated with antithyroid drugs or by subtotal thyroidectomy. During the period from 1908 through 1955 at the Mayo Clinic, 253 children, all less than 15 years of age, had thyroid disease diagnosed as exophthalmic goiter. It was hoped that observations over this 48-year period would add to the understanding of the course of exophthalmic goiter in children, and would help to appraise subtotal thyroidectomy as a method of treating it. There were 217 girls and 36 boys, a ratio of about 6:1. The disease in children does not appear to differ significantly from that in adults, although there is less tendency for children to have severe exophthalmos. Exophthalmos that occurs during childhood may persist for years after thyrotoxicosis has been relieved. Diabetes mellitus is observed more frequently among children with exophthalmic goiter than would be expected as a chance occurrence. Exophthalmic goiter during childhood, if adequately treated, does not alter adolescent development.

Subtotal thyroidectomy is a satisfactory and safe method of treating exophthalmic goiter in children. There were only 4 hospital deaths among 196 children treated in this way. No surgical death has occurred since 1933 among children treated by subtotal thyroidectomy. More extensive resection of the thyroid gland has not eliminated the recurrence of hyperthyroidism. Myxedema, although not considered a serious complication, occurs in a high percentage of patients treated by the extensive subtotal resection of the thyroid gland that is now carried out at the Mayo Clinic. Hypoparathyroidism, keloid formation in the operative scar, and injury to the recurrent laryngeal nerves rarely occurred in the patients of this series. The authors believe that a final evaluation of the best method of treating exophthalmic goiter in children must await an extensive experience with other methods of treatment.

Spontaneous Gangrene in Early Infancy. J. R. Vasquez, A. A. R. Mendilaharzu and J. E. Mosquera. Arch. argent. pediat. 29:152-163 (Sept.) 1958 (In Spanish) [Buenos Aires].

Five infants with spontaneous gangrene were observed in the Hospital de Niños in Buenos Aires between 1950 and 1956. The first, a newborn infant, was hospitalized in a critical condition with gangrene from obstetric trauma and septicemia. He did not respond to penicillin, streptomycin, and vasodilating drugs and died 10 hours after hospitalization. An autopsy showed deep and superficial thrombophlebitis of all veins in the region involved by gangrene. The other 4 patients were between the ages of 3 months and 1 year and, on hospitalization, were in a state of severe dehydration from septicemia, vomiting, and diarrhea. The treatment of these 4 patients consisted of intravenous injections of plasma, cortisone, penicillin, and streptomycin and subcutaneous injections of solutions to control dehydration. One infant with gangrene of the fingers of both hands and another with gluteal and facial gangrene responded well to the treatment; the areas of gangrene became limited, and the scars from necrotic tissue were eliminated, the patients being discharged one month after hospitalization.

The remaining 2 patients (the 4th and 5th of the series) were hospitalized in a very critical condition. The 4th patient had gangrene of the fingers of one hand, meningeal symptoms, and pneumonia. Besides the treatment given to all the patients, she was given intravenous injections of an acetylcholine preparation (Arterocolina), but death occurred 24 hours after hospitalization. No autopsy was granted. The 5th patient had symmetric gangrene of the hands and feet. Radial and tibial posterior pulses were absent. In addition to the treatment given to the other patients, this patient had anesthetization of the splanchnic nerves, and Novocain was used to anesthetize the stellate ganglion, but the child died 10 hours after hospitalization. An autopsy failed to show thrombosis or sclerosis of arteries and veins, but the cubital and radial arteries showed a fibrinoid degeneration. The author states that this case of symmetric spontaneous gangrene of the hands and feet of an infant is the first to be reported in the literature. It suggests an unknown predisposing factor, probably fibrinoid necrosis, which in association with other common causal factors determines this special type of gangrene in infants.

"Maple Syrup Urine Disease": An Inborn Error of the Metabolism of Valine, Leucine, and Isoleucine Associated with Gross Mental Deficiency. D. Y. Mackenzie and L. I. Woolf. Brit. M. J. 1:90-91 (Jan. 10) 1959 [London].

A girl, aged 4 months, with severe mental deficiency was admitted to the Hospital for Sick Children in Oxford. Her condition at birth appeared normal. When one week old she stopped sucking and had to be tube-fed. At 4 months she was noticed to be jerking her limbs and occasionally to become breathless and cyanosed. There was no control of head movements, although she occasionally attempted to follow a bright light with her eyes. A firm liver edge was palpable 1 to 2 fingerbreadths below the costal margin. Lumbar puncture produced a normal cerebrospinal fluid under normal pressure, but the electrocardiogram showed an abnormal record. The urine was examined to exclude phenylketonuria. On smelling a fresh specimen, the similarity to maple sirup was detected. On paper chromatography of the urine, valine, leucine, and isoleucine were found in large amounts. These amino acids were also present in the blood, cerebrospinal fluid, and saliva in great excess. Keto acids were present in the urine in large amounts, as were nonketo acids with the properties of alpha-hydroxy acids. The "maple sirup" smell is due mostly to the alpha-hydroxy acids, though modified by the keto acids. Paper chromatography of the urine for indole derivatives revealed an excessive excretion of indoleacetic and indolelactic acid. The blood true sugar concentration was only 60 mg. per 100 cc. after eating and 52 mg. per 100 cc. on fasting.

The authors suggest that this child has an inborn error of metabolism, and point out that Menkes, Hurst, and Craig in 1954 reported 4 cases, in one family, of severe progressive cerebral dysfunction, associated with the presence in the urine of an organic acid smelling like maple sirup. Also, Westall, Dancis, and Miller in 1957 reported one patient with "maple sirup urine disease," who had raised blood and urine concentrations of valine, leucine, and isoleucine and who in many respects resembled the patient reported here. "Maple sirup urine disease" is not a satisfactory name for the condition. Although one could use, for example, "leucic aciduria," there is no logical reason for picking one rather than another substance in the urine to provide a name for the disease. Since the inborn error of metabolism of the 3 amino acids may be associated with a block at the oxidative decarboxylation stage, "carboxylase deficiency disease" might eventually meet the need for a better term. Tryptophan metabolism is also interfered with, as in the case in patients with phenylketonuria. Differentiation of this condition from phenylketonuria needs special care.

OPHTHALMOLOGY

Presentation of an Unusual Case of Progressive Exophthalmos. R. W. Patterson Jr. and J. E. Campbell Jr. J. Tennessee M. A. 52:13-14 (Jan.) 1959 [Nashville].

The authors report on a 29-year-old woman who had been treated by an otolaryngologist for sore throat of several days' duration. Severe headache occurred, and pain and tearing of the left eye were followed by definite 3-to-4-mm. proptosis of the left eye, with marked edema and tenderness about the left orbit, for which the patient was hospitalized with a diagnosis of retrobulbar abscess. During the initial period of hospitalization large doses of antibiotics were administered, but the course of the exophthalmos rapidly increased in severity. The proptosis and chemosis became extreme. No evidence of thyroid dysfunction could be found. In an effort to halt the progression of the exophthalmos, corticotropin (ACTH) was given in association with desiccated thyroid. The emotional stability of the patient became uncontrollable, and prednisone in doses of 40 mg. daily was substituted for corticotropin. Within several days the proptosis and chemosis began to show definite improvement. On discharge the patient was receiving a daily dose of 30 mg. of prednisone,, and this was gradually reduced to 8 mg. daily. The proptosis disappeared completely 9 months after the initial attack and 2 months after complete withdrawal of the drug. The causation of the exophthalmos in this patient was unknown, but the condition responded dramatically to treatment with prednisone. Cases of progressive exophthalmos may occur in the absence of any demonstrable thyroid abnormality.

Cortical Blindness with Partial Recovery Following Acute Cerebral Anoxia from Cardiac Arrest. W. F. Hoyt. A. M. A. Arch. Ophth. 60:1061-1069 (Dec.) 1958 [Chicago].

The author reports on a 39-year-old woman with cortical blindness resulting from cardiac arrest leading to profound cerebral hypoxia. The patient had suffered multiple stab wounds in the right side of the chest, inflicted with an ice pick by a man with whom she had been living. On admission to hospital, pneumothorax was suspected and confirmed by a chest roentgenogram. During the performance of the x-ray examination the patient suddenly had acute respiratory distress and became unconscious. Within 2 minutes an emergency thoracotomy was performed, and manual massage of the heart was begun. Within 3 to 5 minutes normal heart beat and blood pressure were restored. The pneumothorax was controlled with catheters placed in both chest cavities. To combat the effects of acute cerebral hypoxia, the patient was placed in hypothermia within 2 hours after thoracotomy, and her body temperature was lowered to 88 F (31 C). She remained in deep coma; her pupils were dilated and fixed and did not respond to light. Hypothermia was maintained for 3 days and coma continued for 36 to 49 hours. Hypothermia was discontinued when the patient's pupils responded briskly to light. Within 12 hours she was able to talk readily, and her comprehension was good.

Nine days after the stabbing, the patient was moved to a general hospital ward through crowded corridors and onto elevators. It was reported that she was unable to see the people whose voices she heard around her. At this time neurological examination revealed that her reflexes and general body sensations were intact and that she had no cerebellar signs. However, she was unable to recognize a small hand light in any part of the visual field of either eye, and she could not perceive hand motions, although her pupillary reactions and optic fundi were entirely normal. At this time classical cortical blindness was recognized.

The case of this patient illustrates true cortical blindness as differentiated from blindness arising from more extensive lesions, such as are frequently described under the eponym "bilateral homonymous hemianopsia." The author believes that there are 2 main reasons why the patient had cortical blindness and failed to show signs indicating more extensive cortical damage. These factors are hypothermia and transtentorial shift. Hypoxia influences particularly laminas 3 and 4 of the cortex, and the visual cortex is particularly susceptible (also the motor cortex, basal ganglions, and cerebellum). Profound involvement of the visual cortex, without evidence of involvement of other cortical areas in this patient, suggests that hypothermia may have avoided some of the cerebral damage which characterizes such cases. However, particular vulnerability of the posterior pole of the brain to acute anoxia and, in addition, some degree of transtentorial herniation occurring as a result of swelling (with resultant embarrassment of the blood supply to the visual cortex) may well explain cortical blindness in this patient.

INDUSTRIAL MEDICINE

Clinical Evaluation of Methocarbamol (Robaxin) in an Industrial Facility. C. S. Plumb. Journal-Lancet 78:531-532 (Dec.) 1958 [Minneapolis].

Skeletal muscle spasm is a complaint frequently encountered in industrial medical practice. The industrial physician must attempt to provide sufficient relief, so that the worker can return to his job, but he also must be sure that the worker can perform his duties in a safe manner, for nothing would be gained if side-effects were induced that might render the worker vulnerable to accident or injury. Mephenesin and then zoxazolamine were popular for some time as muscle relaxants, but had shortcomings. This paper is concerned chiefly with methocarbamol (Robaxin), the latest addition in the field of muscle relaxants which has a more extended activity than mephenesin.

Observations are reported on 60 industrial workers who were treated with methocarbamol. These patients encompassed a good cross section of 2,500 workers of a chemical and paper manufacturing industry. Care was taken to include in this study only workers who, on their initial examination, were considered to have uncomplicated skeletal muscle spasm. The minimal dose of methocarbamol necessary for a satisfactory response was found to be 1 Gm. (2 tablets) every 4 hours; smaller doses did not produce the desired results. Fifty-five of the 60 workers could return to full or light duty. The author concludes that methocarbamol reduces muscle spasm without producing side-effects, and that it is a safe drug, which the industrial physician may use with confidence.

Mortality Due to Coronary Disease Analyzed by Broad Occupational Groups. J. M. Mortensen, T. T. Stevenson and L. H. Whitney. A. M. A. Arch. Indust. Health 19:1-4 (Jan.) 1959 [Chicago].

The question whether executive and managerial personal are more likely to die of a coronary heart disease than laborers was the motive for this study based on the mortality rate among male employees of the U. S. Bell Telephone Company. This investigation was carried out over a 5-year period beginning in 1951 and extending through 1955. Deaths were classified according to the International List of Causes of Deaths. A comparison of the death rates of coronary causes and of all causes showed a sharp rise in the proportion of coronary deaths in persons ranging in age from 26 to 40 years. At the age of 40 years the ratio of deaths due to coronary disease and the total deaths was almost the same, staying within the range of 30 to 40% through the age of 60 years. A slight decline appeared at the later age. Active employees, ranging in age from 40 to 64 years, were used for comparison among the different occupation groups. This age group made up more than 375,000 life years of exposure in the 5-year period, and among these workers 1,082 deaths due to coronary causes occurred. In order to make a comparison among the occupations, the employees were classified into groups according to their type of work and the responsibility involved.

The ratio of actual to expected deaths in the group of white-collar workers was 106%, with a probable deviation of ± 3; there is a 50% chance that the true ratio for this group would be between 103 and 109%. A similar range for the group of laborers was from 93 to 99%. Even though the death rate of coronary causes appeared to be higher in the group of white-collar workers, there was no consistency within the groups. The subdivisions of the group of managers, which included officials, supervisors of staff, and foremen, could be classified as pertaining to top, middle, and lower management. The top executives not only showed the lowest level of mortality of the group of managers, but also of the entire group of employees. The high mortality rate of the clerical group was to some extent caused by a transfer of physically impaired craftsmen into this group.

Summarizing the results of this study, it is evident that among male employees of the Bell System there is no substantial difference between the mortality rate due to coronary disease of the top executives and that of craftsmen and laborers, but there is a marked difference between the mortality rate of top executives and that of middle managerial personnel. This fact cannot be explained by these data. The popular notion that top executive positions are associated with a high death rate caused by coronary disease may be attributed to the great publicity connected with these deaths rather than to statistical facts.

THERAPEUTICS

Mechanism of Action of Pyretotherapy in Neurosyphilis: Possibilities of Use in Leprosy. M. B. Moreira. Rev. brasil. med. **15**:624-628 (Sept.) 1958 (in Portuguese) [Rio de Janeiro].

General paresis and tabes dorsalis are controlled by pyretotherapy by a dual mechanism of effects of intermittent marked changes of temperature on Treponema pallidum and a reaction of the reticuloendothelial system with an increased production of phagocytes. In neurosyphilis, pyretotherapy kills T. pallidum or makes it more vulnerable to the effects of antisyphilitic drugs and more amenable to phagocytosis, which is carried out by the large mononuclear cells, the lymphocytes, and the microglia. Neurosyphilis and leprosy are nonfebrile diseases whose causal organisms are susceptible to induced pyretotherapy. Pyretotherapy in leprosy renders Mycobacterium leprae more vulnerable to the effects of the sulfones and more amenable to phagocytosis. A large number of patients with leprosy in the San Roque Colony in Rio de Janeiro have been treated with sulfone compounds after pyretotherapy. This article is a preliminary note, aimed at inciting interest in the possibilities of pyretotherapy in leprosy. The results up to now have been very promising.

The Protein-Sparing Effect of Androgenic Hormones After Gastrectomy. R. G. A. van Wayjen, J. Groen and A. F. Willebrands. Nederl. tijdschr. geneesk. **102**:2413-2422 (Dec. 6) 1958 (In Dutch) [Amsterdam].

The utilization of proteins was investigated by means of balance studies in 31 patients who had been subjected to gastrectomy. The amount of food eaten was carefully weighed, and, in order to determine the utilization of proteins by the body, the nitrogen content of the urine and feces and the fat content of the feces were ascertained. The balance studies required from 10 to 45 days. A total of 41 balance studies were carried out, some patients being subjected to more than one. Thirteen of the patients were treated with androgenic hormones, and 18 were not. The utilization of proteins improved in all except one of the male patients treated with androgenic hormones in the form of testosterone propionate. A lower dose of testosterone propionate combined with estrogens improved the nitrogen balance in a female patient.

Comparison of the calorie intakes and of the body weights of the patients while they were in the hospital revealed that those receiving hormone treatment consumed an average of 2,355 calories a day and gained an average of 3.9 kg. (8½ lb.) in weight over a period of 30 days; the respective figures for the 18 patients not receiving hormone therapy were 2,740 calories and 1.4 kg. (3 lb.). Thus, the treatment with androgenic hormones was accompanied by a greater weight increase. Furthermore, the increase in weight continued when, after discharge from the hospital, the patients were given maintenance doses of testosterone phenyl propionate. The androgenic hormone therapy caused no unpleasant side-effects. The authors feel that androgenic hormone therapy can be recommended for patients whose nutritional status is impaired as the result of total or partial gastric resection.

Chlorothiazide (Chlotride) as Part in Treatment of High Blood Pressure. H. S. Mathisen and D. Jensen. Tidsskr. norske lægefor. **78**:1230-1231 (Dec. 15) 1958 (In Norwegian) [Oslo].

Sixty patients (27 men and 33 women) with hypertension were treated with chlorothiazide for an average of 6.2 months. The agent was administered by mouth in 0.5 Gm. tablets, and seldom more than one tablet was given daily. Often the dose was reduced to one-half tablet daily, given after breakfast and with 1 or 2 days' interlude during the week on long-term treatment. Except in one case, chlorothiazide was combined with one or several other hypotensive medicaments with which the patient had been treated for some time. In the combined hypotensive treatment, the dosage of the other hypotensive substances was unchanged, except in the case of ganglion-blocking agents whose doses were usually cut in half. Chlorothiazide taken by mouth in doses of 0.25 to 0.5 Gm. not only has a diuretic effect but also reduces the blood pressure in hypertensive patients. In these doses chlorothiazide increases the effect of other hypotensive agents (hydralazine, rauwolfia, protoveratrine, and ganglion-blocking agents). Patients who have undergone sympathectomy are sensitive to chlorothiazide treatment. The agent is well borne, with minimal side-effects, and is regarded as valuable in the medicinal treatment of high blood pressure.

Antibacterial Effect of Ristocetin. A. Farulla, A. Cassano, L. Nuzzolo and G. Giordano. Riforma med. **72**:1353-1355 (Nov. 29) 1958 (In Italian) [Naples].

A study in vitro on the antibacterial effect of ristocetin is reported on. The antibiotic used in the study contained component A and component B of ristocetin in a proportion of 70 and 30% respectively. The minimum concentration of ristocetin necessary to inhibit the growth of Micrococcus (Staphylococcus) pyogenes var. aureus was 4.5 mcg. per milliliter; in some cases, though, it was 9.4 mcg. per milliliter. The minimum inhibitory concentration values obtained in tests with hemolytic streptococci and streptococci of the viridans group ranged from 0.3 to 1.2 mcg. per milliliter. Marked sensitivity was noticed in tests with Streptococcus faecalis and Diplococcus pneumoniae. Ristocetin had no antibacterial effect on gram-negative bacteria, but all gram-positive bacteria from recently isolated strains were sensitive to the drug. Fifty strains of M. aureus, 10 of hemolytic streptococci, 10 of Str. faecalis, and 10 of D. pneumoniae showed 100% sensitivity to ristocetin, and no natural resistance was noticed. All the strains of hemolytic streptococci, Str. faecalis, and D. pneumoniae were 100% sensitive to such other antibiotics as penicillin and tetracycline, while M. aureus showed a 42% sensitivity to penicillin and a 96% sensitivity to tetracycline.

PATHOLOGY

Pleural Biopsy in the Diagnosis of Pleural Effusion: A Report of 200 Cases. P. Mestitz, M. J. Purves and A. C. Pollard. Lancet 2:1349-1353 (Dec. 27) 1958 [London].

The authors performed 228 punch biopsies of the parietal pleura, using the Harefield needle, on 200 patients, between the ages of 3 and 85 years, most of whom had an effusion at the time of the investigation. One hundred seventy-four patients had one biopsy, 24 patients had two, and 2 patients had three. Biopsy established the diagnosis by determining the cause of the effusion in 80% of the patients with tuberculous effusions and in 60% of those with malignant effusions. Pleural punch biopsy proved to be by far the most reliable diagnostic technique in patients in whom tuberculosis was suspected. Only one of the diagnoses made with the aid of the 228 biopsies proved to be wrong. Pleural punch biopsy may be the only way of making a definite diagnosis during life. Trivial complications consisted of subcutaneous hematoma in one patient and a small pneumothorax in another patient. Pleural punch biopsy is a simple and safe method which should be part of the initial investigation of every patient with a pleural effusion of uncertain causation.

Ossifying Bronchial Adenoma. C. P. Thomas and A. D. Morgan. Thorax 13:286-293 (Dec.) 1958 [London].

It is generally conceded that bronchial adenoma is a benign epithelial tumor of mucous glands, with a cylindromatous variant of low-grade malignancy, but the "mixed tumor" theory still has adherents. The occasional presence of bone in the growth is usually attributed to metaplasia of the stroma. The frequency with which ossification occurs in bronchial adenomas is difficult to assess. Between 1939 and 1958, 63 cases of bronchial adenoma were treated by resection by one of the authors. Widespread ossification of the type dealt with by the authors was mentioned by the pathologist in only 3 cases, which are described in this paper. The authors conclude that bone formation in tumors is due to a metaplasia of the stroma brought about by multiple factors. Its relative frequency in bronchial adenomas is due in part to slow growth, but principally to the presence of cartilage in or near the tumor. The cartilage undergoes necrosis and calcification and affords a convenient medium for ossification. Where distant metastases of malignant epithelial tumors are ossified, the metaplasia is probably due to a chemical influence exerted by the tumor cells themselves.

The Effect of Hypercalcemia Induced by Calciferol upon Renal Concentrating Ability. F. H. Epstein, M. J. Rivera and F. A. Carone. J. Clin. Invest. 37:1702-1709 (Dec.) 1958 [New York].

Polyuria and loss of renal concentrating ability have frequently been observed in patients with hypercalcemia. It has not been clear whether the capacity of the kidneys to concentrate urine is selectively impaired by hypercalcemia or whether it is depressed, together with many other renal functions, as a result of injury to and encroachment upon active renal parenchyma. In the experiments described, the effects of hypercalcemia on renal function and morphology were studied in rats given large doses of calciferol (vitamin D_2) for several days. Hypercalcemia was induced in rats by 4 daily injections of 200,000 to 400,000 units of calciferol. Renal concentrating ability was markedly impaired, although there was little or no change in blood urea, urea clearance, or the excretion of phenolsulfonphthalein. Morphologic changes in the kidneys were sparse and consisted chiefly of lesions involving the collecting ducts in the outer medulla. It is suggested that similar alterations in renal structure and function may be responsible for the polyuria and hyposthenuria observed in a variety of clinical states associated with hypercalcemia or nephrocalcinosis.

RADIOLOGY

The Advantages and Limitations of Cobalt 60 Hectocurie Teletherapy. N. Simon and S. M. Silverstone. Am. J. Roentgenol. 81:38-42 (Jan.) 1959 [Springfield, Ill.].

The authors feel that occasional bursts of enthusiasm by the lay press distort and exaggerate the benefits derived from radio cobalt (Co^{60}) teletherapy, but the radiotherapist realizes that the true value lies somewhere between the exaggeration of the lay press and the iconoclasm of the over-conservative radiologist. The beneficial features of Co^{60} teletherapy include: (1) skin sparing; (2) increased depth dose; (3) lessened bone absorption; (4) decreased side-scatter; and (5) simplicity of operation. Skin sparing of the Co^{60} beam is by far its most advantageous characteristic. It allows high dosage through single portals, and sometimes this skin sparing provides access with radiation to lesions which are not usually considered treatable. For example, carcinoma of the rectum, either the postoperative recurrence or the locally unresectable lesion in the hollow of the sacrum, is difficult to treat unless the skin over the sacrum can be spared.

Although increased survival may be too much to expect, palliation and control of bleeding are more often achieved with Co^{60} teletherapy than with irradiation in the "conventional" range. The lessened bone absorption with Co^{60} teletherapy increases the dose to tissues beneath bone, such as brain and pelvic organs, and it is also possible that radionecrosis of bone may be lessened. The decreased side-scatter of the Co^{60} beam is presumed to account for lessened radiation sickness. The experience of these authors in the treatment of 600 patients with a Co^{60} hectocurie unit in the past 3 years bears out this presumption. Finally, a Co^{60} hectocurie apparatus is far simpler to operate than a 200-kv. or supervoltage roentgen-ray machine.

The authors discuss the following disadvantages of Co^{60} hectocurie therapy in comparison with 200-kv. roentgenotherapy: (1) unsuitability for intraoral (and intravaginal) therapy; (2) unsuitability for treatment of skin cancer; (3) reduced usefulness of the large fields; (4) too much penumbra at long-source skin distances; and (5) requirement of radiation protection of operating personnel. The use of electron filters to help in the design of cones, particularly for treatments at short-source skin distances with the hectocurie units, is discussed. There are two advantages to the use of short-source skin distances: (1) increased output and (2) rapid dose fall-off. These advantages can be obtained, while still retaining the skin-sparing feature of Co^{60} teletherapy, by closing the end of the cone with a thin sheet of brass.

An important lesion deserving special comment in relation to Co^{60} hectocurie teletherapy is carcinoma of the larynx. Early results in 30 patients indicate as favorable a response as the best obtained with 200-kv. roentgenotherapy. In addition, the patient has no skin discomfort, and after a few months the epilation is the only identifying characteristic of the skin treated. If laryngectomy is indicated for persistence or recurrence of the lesion after Co^{60} treatment, healing of the operative wound will not be seriously hampered. The relatively low morbidity, the retention of voice, and the comparatively satisfactory "cure" rate render Co^{60} hectocurie teletherapy the treatment of choice in lesions confined to the larynx.

Zinc-65 in Foods and People. R. W. Perkins and J. M. Nielsen. Science 129:94-95 (Jan. 9) 1959 [Washington, D. C.].

Trace amounts of radiozinc (Zn^{65}) are disposed in the Columbia River via Hanford reactor effluent water. The subsequent utilization of river water for irrigation permits concentration of this radioisotope in farm produce and its eventual deposition in man. The authors report on measurements of Zn^{65} in irrigation water, in farm produce, and in individuals utilizing these materials. The farm-produce and animal samples considered here were obtained from an irrigation project about 30 miles downstream from the Hanford reactors. By means of gamma-ray spectrometric techniques, measurable amounts of Zn^{65} were found in all the farm produce sampled from this location. The Zn^{65} concentrations found in milk, beef, and various vegetables from this land are shown in a table. The fact that the pasture grass contained a relatively high Zn^{65} concentration, as compared with the vegetables, is probably related to both the manner and the amount of irrigation, as well as to the fact that some difference in uptake exists between leaf and fruit portion of plants. The pasture grass was irrigated almost continuously, while the vegetables were irrigated only a few times during their growing season. In addition, the Zn^{65} may enter the grass by foliate absorption during irrigation as well as through the soil.

The relatively high Zn^{65} concentration in milk, as compared with that in pasture grass, indicated that a large amount of Zn^{65} is taken from the feed into the blood stream of the cow and translocated into the milk. The low Zn^{65} concentration found in beef samples may be explained by the fact that the animal in question was slaughtered in late winter and had been fed on essentially Zn^{65}-free foodstuffs for 3 or 4 months prior to that time. The Zn^{65} concentration in flesh, fat, and bone samples of another beef animal, which had spent its entire life in the same location, was about twice that in the first animal in the previous year. It was also observed that hair, liver, and bone concentrate zinc to a greater extent than other organs.

The gamma-ray spectrum of an individual who consumed approximately 0.1 and 0.7 kg, respectively, of meat and milk per day from the source mentioned is shown in a figure. Measurements were made in 12 other persons whose diet did not include food from the irrigation project but did, in some cases, include drinking water from the Columbia River. The presence of Zn^{65} in the amounts observed in no way constituted a hazard. Even the amount in the individual whose diet included meat, milk, and drinking water from the project was less than 0.01% of the total permissible body burden for this isotope. Also, even the highest Zn^{65} value in pasture grass was less than 5% of the maximum permissible concentration for human foods.

Irradiation of the Entire Body and Marrow Transplantation: *Some Observations and Comments.* E. D. Thomas, H. L. Lochte Jr. and J. W. Ferrebee. Blood 14:1-23 (Jan.) 1959 [New York].

The authors mention previous experimental and clinical studies on whether infusion of normal bone marrow will induce recovery after exposure to irradiation that otherwise would prove fatal. They point out that there are dissimilarities between man and lower animals that make translation of the experimental data difficult. In this communication they present further clinical experience with whole-body irradiation and marrow transplantation by presenting the histories of 5 patients with acute leukemia who received total-body irradiation and intravenous infusion of normal marrow. An 8-month follow-up on a previously reported patient with chronic leukemia is included, and a review of the case of a person receiving nitrogen mustard and marrow is presented. Of several patients reported in this and in a previous communication, only 2 may be said to have obtained significant clinical benefit.

Possible reasons for this low incidence of improvement are suggested, and the difficulties involved in total-body irradiation and marrow replacement in man are discussed. The authors mention the difficulties in cell division resulting from ionizing radiation and the involved cessation of *production of the circulating formed elements:* platelets, leukocytes, and erythrocytes, which, in turn, is followed by bleeding and infection. Other problems discussed are possible immunological reactions to marrow transplantations, the number of cells required and obtainable from fetuses and from cadavers, the use of spleen, the time after irradiation at which marrow should be administered, and the technical difficulties involved in total-body irradiation.

Carotid Angiography in the Localization of Supratentorial Neoplasms and Hamartomata. P. F. J. New. Radiology 72:35-41 (Jan.) 1959 [Syracuse, N. Y.].

In an attempt at assessment of the value of carotid angiography in the localization and diagnosis of supratentorial neoplasms and hamartomas, the author reports on 131 supratentorial neoplasms and arteriovenous malformations studied and verified between 1952 and 1957. Of the 131 lesions, 130 were examined by carotid angiography, and in 35 of these pneumography (encephalography and/or ventriculography) was employed in addition to angiography. Only one lesion was studied by encephalography alone. Of the 131 lesions, 88 (48.4%) were gliomas, 14 were meningiomas, 11 were metastases, and 18 were arteriovenous malformations. The results of these studies showed that cerebral angiography may be safer and less disturbing to the patient than pneumography. It is *less time-consuming* than a properly conducted pneumographic study.

It is postulated that most of the supratentorial space-occupying lesions are best examined first by carotid angiography. This method alone will frequently provide a pathological diagnosis in addition to a satisfactory localization, judged by the presently accepted criteria of accuracy. A high *proportion of avascular space-occupying lesions* will be accurately localized; most of the exceptions will be tumors limited to the occipital or parietal lobes, to the deep central portions of the hemispheres, or very early, small lesions. In a moderate number of cases additional pneumography, usually encephalography, will be required to provide additional information regarding the site and extent of the lesion. Unfortunately very extensive infiltrating gliomas can occasionally exist with no definite angiographic or pneumographic abnormality. A negative angiogram in the presence of reasonable clinical suspicion of a neoplasm should lead to pneumography, either within a few days, if the index of suspicion is relatively high, or within a few weeks, if suspicion is not so great initially but symptoms and signs are progressive. Suspected midline basal neoplasms are best investigated in the first instance by pneumography unless a meningioma or other vascular mass is suspected. The present aim is to use very rapid serial angiography to provide more detail of the circulation of the tumor and to employ angiography combined with pneumography in more and more cases, as the presently accepted criteria of accuracy of localization are not felt to be satisfactory.

BIOCHEMISTRY

The Immediate Effect of Hypophysectomy and Section of the Pituitary Stalk on the Urinary Steroid Excretion in Man. B. Hökfelt, R. Luft, D. Ikkos and others. Acta endocrinol. 30:29-36 (Jan.) 1959 (In English) [Copenhagen].

The urinary excretion of steroids, including aldosterone, was studied immediately after operation in 2 men who had been subjected to hypophysectomy because of metastasis of malignant melanoma and in a woman in whom the pituitary stalk had been sectioned because of carcinoma of the thyroid with metastases. For evaluation of the steroid hormone production the 24-hour urinary output was collected without preservative, and stored in the refrigerator. Hypophysectomy was found to result in the disappearance of nonconjugated cortisol and cortisone, as well as of the corresponding tetrahydro derivatives. In agreement with this, there was a rapid and marked decrease in total 17-ketogenic steroids. Sectioning of the pituitary stalk was found to produce an increase in the urinary output of these metabolites. Changes parallel to those in 17-ketogenic steroids were observed in the 17-ketosteroids. An increase in the urinary excretion of aldosterone was found in all 3 patients.

The Biology of Metacorticoid Hypertension. F. M. Sturtevant. Ann. Int. Med. 49:1281-1293 (Dec.) 1958 [Lancaster, Pa.].

The search for effective treatment of essential hypertension has led to the laboratory exploration of many contributing factors, and 4 major types of experimental hypertension: neurogenic, renal, renoprival, and hormonal have been chiefly investigated. Green in 1953 and 1954, while reviewing the similarities and differences among human and experimental hypertensions, concluded that essential hypertension in human subjects is simulated most closely by the post-DOCA (desoxycorticosterone acetate) or metacorticoid syndrome. The author reviews all available information on this syndrome, pointing out that metacorticoid hypertension is a self-sustaining disease that is no longer dependent upon a continuing overdosage with DOCA and dietary sodium. The term "metacorticoid" in place of "post-DOCA" or "self-sustaining" was suggested by Selye, who likened this condition to the "metahypophysial" and "metathyroid" diabetic states described by Houssay.

Metacorticoid hypertension is produced in this author's laboratory by the subcutaneous implantation in 75-Gm. male rats of an extruded pellet containing a 2:1:1 mixture of DOCA, Carbowax 4000, and Flexowax C Light. Each pellet weighs 40 mg. Immediately after implantation, the rats are offered only 0.86% sodium chloride solution as drinking fluid, and are kept for a 3-month waiting period, after which they are considered to be "metacorticoid." The pellet remnants at this time contain only 0.2 to 0.3% of the original amount of DOCA.

The author concludes that metacorticoid hypertension is a self-sustaining disease in rats that is produced by temporary overdosage with DOCA and sodium. It may be characterized by an exaggerated urinary excretion of sodium and water, which is related to the duration of the disease, the sodium and water intake, and the blood pressure level. The urinary sodium/potassium ratio is elevated. When the rats are offered only isotonic sodium chloride solution or water to drink, there is a relative polydipsia; when they are offered a free choice between the two, a relative aversion to the sodium chloride solution is exhibited. The life expectancy of the metacorticoid rat is greatly reduced, although individual rats may live a year or more after DOCA implantation. The elevated blood pressure, cardiovascular reactivity, vascular lesions, disturbances in salt and water metabolism, and decreased life expectancy appear, to some extent, to be independent of each other. The maintenance of the disease is dependent upon the pituitary, the thyroid, and the kidney. Clinically active drugs cause transitory decreases of blood pressure in metacorticoid rats, although seemingly huge doses are often required.

Ionised, Protein-Bound, and Complexed Calcium in the Plasma in Primary Hyperparathyroidism. H. M. Lloyd and G. A. Rose. Lancet 2:1258-1261 (Dec. 13) 1958 [London].

Calcium is present in plasma in the ionized, complexed, and protein-bound states. Although the 3 fractions are believed to be in equilibrium with one another, the level of the ionized calcium is regarded as the one most immediately related to the activity of the parathyroids. The authors report the results of measurement of the plasma calcium fraction in 17 patients with primary hyperparathyroidism. They are especially concerned to note the value of these measurements for the diagnosis of the disorder. In 16 of the 17 patients the condition was shown to be due to a single chief-cell adenoma, which was removed. In the remaining patient explorations of the neck and mediastinum were negative, but the diagnosis was not in doubt. The level of ionized calcium in the plasma was raised before operation in every patient, except one who was probably in temporary remission. After removal of the adenoma the level of ionized calcium always fell to normal or below normal; this fall was proportionately greater than the fall in the protein-bound fraction. It was inferred that the parathyroid hormone reduces the ability of the plasma proteins to bind calcium.

As a result of investigations on the patients, it was considered desirable to investigate the effect of administering parathyroid hormone to a healthy volunteer. Accordingly, the plasma calcium fractions were measured before and after 5 intramuscular injections of 400 U.S.P. units of Parathormone given at intervals of approximately 12 hours. Observations on this volunteer corroborated that parathyroid hormone reduces the ability of plasma proteins to bind calcium. It has been observed that it is possible for patients with normal total plasma calcium and with normal plasma proteins and pH to have a high ionized fraction. In such cases measurement of the ionized calcium in the plasma is a most valuable diagnostic aid. This measurement is also a valuable screening test for patients with "idiopathic hypercalciuria" in order to exclude primary hyperparathyroidism. If the level of ionized calcium in the plasma is raised, the hypercalciuria is not "idiopathic."

PUBLIC HEALTH

Second Chest X-Ray Survey of the Population of Amsterdam. A. Kalthofen, B. van Vliet and J. van der Zee. Acta. tuberc. scandinav. 36:141-151 (no. 2-3) 1958 (In English) [Copenhagen].

A second chest x-ray survey was carried out on the population of Amsterdam between June, 1954, and August, 1957. Only persons over 14 years of age were included. The results of this second survey were compared with those of the first one carried out between April, 1951, and May, 1954. Among the 400,959 persons examined, 179 were found to have no previously detected pulmonary tuberculosis. In the first survey in which 411,111 inhabitants were examined, 379 persons with formerly unknown active pulmonary tuberculosis were detected. This was practically a 100% decrease; the number detected was smaller by 200, whereas the number of persons examined was only slightly smaller. Although the number of females examined was 12% larger than the number of males, the incidence of tuberculosis among females was lower by 58%. The maximal number of cases of tuberculosis was found among males of the age group 40 to 49, while the minimal number was found among females in the age group 50 to 59.

Pulmonary tumors were demonstrated in 185 persons during the second survey, that is, tumors were more numerous than tuberculosis. The 185 tumors included 19 that were benign, 31 that were suspected of possible malignancy, and 135 that were definitely malignant tumors. There were 96 patients in whom bronchial carcinoma had been clinically demonstrated; 24 of these had been operated on with good early result. In the first survey 176 pulmonary tumors (including 135 malignant ones) had been demonstrated.

A Rapid Test for Detecting Staphylococcus aureus in Food. E. Wilson, M. J. Foter and K. H. Lewis. Appl. Microbiol. 7:22-26 (Jan.) 1959 [Baltimore].

Coagulase-positive staphylococci are responsible for approximately 75% of the food-borne illnesses of established etiology that have been reported in the United States during recent years. To determine the relation of a suspected food to staphylococcic food poisoning, the presence of enterotoxin should be demonstrated, but the methods available for this purpose are cumbersome. In lieu of demonstrating enterotoxin, a rapid method has been developed for detecting the bacteria that are known to produce enterotoxin, that is, the coagulase-positive staphylococci. The method allows detection of Staphylococcus pyogenes var. aureus in food within a 7-to-9-hour period. A selective culture technique in brain heart mannitol salt broth has been combined with the growth-accelerating effect of agitation in air during incubation. After the incubation with shaking of 4 to 6 hours at 35 C, the broth culture is used for a gram-stained preparation and for the coagulase test. Modifications of the method are proposed for use when circumstances preclude completion of the entire procedure in a single working day.

Studies were performed with experimentally contaminated ham, custard, creamed chicken, and milk. When Staph. aureus was present in these foods in pure culture, it was detected in 7 to 9 hours at levels ranging from 2,200 to 48,200 per gram, depending upon the food examined; whereas in the presence of 4 million to 15 million aerobic sporeformers per gram, staphylococci were detected at levels ranging from 17,000 to 43,500 in custard, and 19,000 to 167,500 in ham. In the presence of enterococci, salmonellae, and aerobic sporeformers totaling 105 million per gram, staphylococci were detected at the level of 235,000 per gram in a 9-hour total test period. These data indicate that the rapid test permits detection of Staph. aureus well below the level cited in the literature as the threshold for the production of sufficient enterotoxin to induce symptoms in man. Principal advantages of this new test are its speed, simplicity, and the ready availability and low cost of the equipment required. Speed of the test is important in relation to epidemiologic investigations of food poisoning outbreaks, and the relative simplicity of the procedure makes it a feasible quality control test for commercially prepared nonsterile foods. The test has not as yet been used for clinical materials.

The Age Factor in Postvaccinal Encephalitis. K. Berger and F. Puntigam. München. med. Wchnschr. 100:2042-2043 (Dec. 26) 1958 (In German) [Munich, Germany].

Investigations were made in Austria on the incidence of postvaccinal encephalitis in relation to the age of the child at the first vaccination. It was found that this complication of vaccination not only shows a general increase among children who are vaccinated for the first time after the age of 3 years, in comparison with children who are vaccinated before they are 3, but the incidence rises further in successive age groups. The grouping according to age of 32 children in whom postvaccinal encephalitis developed during 1948-1953 and the grouping of the 69,706 vaccinations according to the ages of the children showed that, whereas in children vaccinated for the first time under 3 years of age 1 case of postvaccinal encephalitis developed in 9,958 children, for the age group of 4 to 5 years it was 1 case in 1,628, for the age group of 6 to 10 years it was 1 in 430, and for the age group of 11 to 14 years it was 1 in 85.

BOOK REVIEWS

New and Nonofficial Drugs: Containing Descriptions of Therapeutic, Prophylactic and Diagnostic Agents Evaluated by the Council on Drugs of the American Medical Association, 1959. Annual publication issued under direction and supervision of Council. Cloth. $3.35. Pp. 687. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6, Canada, 1959.

This book contains monographs on drugs which have been evaluated on the basis of available scientific data by consultants and members of the A. M. A. Council on Drugs. It begins with a statement of the principles governing the evaluation of the drugs which are described. The 1959 edition includes new Council monographs that have appeared in The Journal since the 1958 edition. Monographs on drugs which either have been included in the book for 20 years or are no longer commercially available have been deleted. The current edition contains approximately 500 monographs, of which 42 are new. A generic listing of available preparations and their strengths and sizes is given with each monograph. Trade names are listed at the end of each monograph and also in the index. Among the important new monographs are those for anileridine hydrochloride, dextro propoxyphene hydrochloride, iproniazid phosphate, oleandomycin phosphate, prochlorperazine, and ristocetin. In view of its admirable coverage of newer drugs, whether or not their usefulness has been established, all physicians and students of medicine should consider the purchase of this annual publication as a guide to drug therapy.

Television in Science and Iudustry. By V. K. Zworykin, E.E., Ph.D., D.Sc., E. G. Ramberg, Ph.D., and L. E. Flory, B.S. Cloth. $10. Pp. 300, with illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1958.

The authors explore the function of closed-circuit or industrial television and describe the tools which have been developed to realize it. A brief historical introduction in the first chapter covers the various attempts to televise in the prescientific era, developments during the era of speculation, and final emergence into the mechanical and electronic era. In chapter 2 the principal applications of television in industry, research, medicine, education, commerce, military affairs, and home and farm work are outlined. In chapter 3 the equipment which has been developed for closed-circuit television is described in detail, including the design and circuitry of the more conventional camera equipment, the miniaturization made possible by the transistors and 0.5-in. vidicons, the operation of color and stereo-television apparatus, and the television microscope.

In chapter 4 the status of closed-circuit television in 1957 is reviewed and examples are cited from actual practice in sufficient detail to enable the reader to judge the situations known to him in which closed-circuit television could be most effective, what equipment would be needed, and how it should be used. Complete references are given to the technical literature. In chapter 5 an attempt is made to forecast the future development of closed-circuit television, with a comparison of performance limits of vidicon and flying-spot television microscopes in the ultraviolet given as an appendix.

The reader of this book should receive an excellent basic education covering the birth, development, and growth of television. He should also become familiar with the many and varied uses of this versatile medium as it has been put to work in science and industry. The section on microscopy is especially detailed and contains valuable reference sources. The discussion of permanent and portable television apparatus as used in medicine is also quite complete for the period covered. Unfortunately, the speed in development and refinement of television apparatus in the past two years somewhat dates this book, but for those who are planning to enter the field of television it should serve as an excellent foundation. This book will be of primary interest to those who would like to familiarize themselves with the technical aspects of television.

Diseases of Children in the Subtropics and Tropics. By H. C. Trowell, O.B.E., M.D., F.R.C.P., Senior Specialist Physician, Pædiatric Unit, Mulago Hospital and Makerere College, University College of East Africa, Kampala, Uganda, and D. B. Jelliffe, M.D., M.R.C.P., D.C.H., Visiting Professor of Tropical Medicine, Tulane University, New Orleans. Cloth. $18.50. Pp. 919, with illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41-43 Maddox St., London, W. 1, England, 1958.

Most of the world's children are born and live in the subtropics and tropics. One would suppose that special textbooks dealing with the problems of these children would be available, but such is not the case. Most of those who are concerned with pediatrics in tropical areas have either been trained in the West or have studied textbooks written from the standpoint of Western medicine. The authors have prepared this volume, with the

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

assistance of about 70 contributors from all over the world, to meet an obvious need. Some of the communities in which these contributors work are Madras, India; London; Sydney, Australia; Uganda; Lagos, Nigeria; Manus, New Guinea; Buenos Aires; Colombo, Ceylon; Paris; Singapore; Bogotà, Colombia; Calcutta; Dakar, South Africa; Jamaica; Kenya; New Orleans; and Washington, D. C.

This book covers the broad field of diseases of children, but it does not attempt to be another standard textbook of pediatrics. Those maladies which are cosmopolitan, such as the infectious diseases of childhood and the commoner disorders of the respiratory and nervous systems, are presented briefly, and attention is called to unusual characteristics which may be due to the tropical environment. Numerous conditions which appear almost exclusively in the tropics and which a pediatrician in the temperate zones would rarely if ever see are described in detail. Among these are kwashiorkor, tropical eosinophilia, paragonimiasis, cholera, Indian childhood cirrhosis, veno-occlusive disease of Jamaica, maduromycosis, yaws, pinta, leprosy, African and Brazilian trypanosomiasis, visceral leishmaniasis, schistosomiasis, loiasis, dracontiasis, and vomiting sickness of Jamaica.

Much space is devoted to such factors that tend to alter or aggravate disease processes as poverty, illiteracy, ignorance, overwork, local superstition, heat, humidity, and malnutrition. These forces are met to some extent in the temperate zone, but the violence of their impact on the health of children cannot be appreciated until one reads of their influences in the tropics. The material is presented in interesting, readable form. Since most of the contributors were trained in British schools, the style is distinctly British and altogether charming. This telling description of a child with kwashiorkor is an example: "an unpleasant picture of unwanted misery." The book is well illustrated, and the various chapters give a brief but adequate list of references. This book should be required reading for physicians who deal with children in the subtropics and tropics. It could also be read with profit and pleasure by any physician who is interested in pediatrics in its broadest sense.

Grosse Nervenärzte. Band 2: 22 Lebensbilder. *In Gemeinschaft mit E. H. Ackerknecht et al. Herausgegeben von Kurt Kolle. Cloth. 29.40 marks; $7. Pp. 251, with 24 illustrations. Georg Thieme Verlag, Herdweg 63, (14a) Stuttgart, West Germany; [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.*

This is a sequel and companion to an excellent book reviewed in The Journal of May 19, 1956, page 294. The present volume offers biographies of Golgi, Nissl, Alzheimer, Brodmann, Cécile and Oskar Vogt, Helmholtz, Quincke, Esquirol, Meynert, Wernicke, Meyer, Gaupp, Marie, Babinski, Head, von Economo, Horsley, Dandy, Vincent, Dubois, and Simon. Each biography is the work of an author who is himself distinguished as a neurologist or psychiatrist, and those chapters which were originally written in English or French appear here in German. A concluding chapter sketches the development of institutions for teaching and research in neurology and psychiatry in France, Great Britain, Italy, Russia, Switzerland, Belgium, Holland, Scandinavia, Spain, and Portugal. Each chapter is illustrated with a portrait of the subject and closes with a brief bibliography. There is an index of names.

Thanks to both a felicitous choice of contributors and painstaking coordination by the editor each chapter gives not only an instructive account of the subject's scientific work but also an interesting picture of his personal life. In connection with the former there is enough detail, accurately presented by an authority, to make the book valuable to students interested in the development of fundamental ideas in scientific medicine. Examples are the thinking and experiments of Helmholtz on the nature of the nervous impulse and the growth of the idea of occupational therapy in the institutional practice of Simon. In connection with personal lives there are innumerable episodes and oddities, all related with tact and understanding. Examples taken at random are Calmiel's deception of Esquirol with a feigned grand mal seizure, Cushing's unfortunate remark that is believed to have started a life-long hostility between him and Dandy, John Horsley's unwillingness to paint from nude models, and Wernicke's enthusiasm for bicycle trips that led to a fatal collision with a lumber wagon in the Thuringian forest. This book is recommended especially to students of neuropsychiatry and of the history of medicine.

Pictorial Handbook of Fracture Treatment. *By Edward L. Compere, M.D., F.A.C.S., Professor and Chairman of Department of Orthopaedic Surgery, Northwestern University Medical School, Chicago, Sam W. Banks, M.D., F.A.C.S., Associate Professor of Orthopaedic Surgery, Northwestern University Medical School, and Clinton L. Compere, M.D., F.A.C.S., Associate Professor of Orthopaedic Surgery, Northwestern University Medical School. Fourth edition. Cloth. $7.50. Pp. 448, with 268 illustrations, line drawings by Harold Laufman, M.D., F.A.C.S., and Jean McConnell. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1958.*

This edition contains many changes in text and in thought from previous editions, and it represents a distinct advance over earlier volumes. The fracture treatment outlined is simply worded, direct and to the point, and amply illustrated. There are a minimum of those roentgenograms which so often are difficult to interpret when reproduced. The technique and methods explained are the standard ones generally in use throughout the United States. There is little attempt on the part of the authors to emphasize favored treatments of their own in certain fractures. They have in some instances described several methods of treating the same problem, but these methods are sound throughout and simply represent variations in technique that may be used to gain the same end.

This handbook is excellent for teaching purposes at the levels of both the medical student and the surgeon interested in orthopedics. It should be in the library of every general practitioner as well as that of the orthopedist. The table of contents shows excellent organization, beginning with some introductory remarks on fractures and their pathology with special reference to healing, and going on to diagnosis, emergency treatment, definitive treatment, and principles of care. The latter two-thirds of the book is so organized that one can turn to the part of the body involved and quickly find the type of fracture in which one is interested. Minor points of dispute might be raised on the discussion of the common ankle fractures, since there is a growing tendency throughout the country to perform open reduction and internal fixation more frequently than the writers advocate. Their conservatism in treating this problem gently is to be recommended, however, since what is standard practice in the hands of the expert is not always feasible in the hands of the general practitioner. This handbook is highly recommended to all traumatic and orthopedic surgeons and to students who are interested in fractures.

The Pneumoconiosis Problem: With Emphasis on the Role of the Radiologist. By Eugene P. Pendergrass, M.D., Professor of Radiology, University of Pennsylvania School of Medicine, Philadelphia. Cloth. $6.75. Pp. 146, with 53 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This book contains the entire manuscript of the Caldwell lecture which the author gave at the annual meeting of the American Roentgen Ray Society, Oct. 1, 1957. It is not a complete treatise on pneumoconiosis. Many phases of the problem of silicosis, asbestosis, and coal workers' pneumoconiosis are not considered. The effort has been directed largely toward a discussion of guide lines helpful in the interpretation of shadow patterns in the roentgenograms. These were gathered from records of silicosis in some 500 workers in industry who were exposed to free silica with essentially no contaminating dust. Many cases were followed up for over 20 years.

This book is aimed at interesting more radiologists in pneumoconiosis. The radiologist not only plays an important role in the diagnosis but also has increased opportunities for estimating pulmonary disability and complementing pulmonary physiological studies. The specific lesions of the three pneumoconioses are described, with emphasis on the necessity of evaluating shadows produced by blood vessels which simulate the pattern of nodulation. Many of the lesions of various forms of pneumoconiosis are not pathognomonic in themselves and simulate other diseases such as tuberculosis and Boeck's sarcoid. The roentgenographic appearance of the various pathological lesions is fully discussed and correlated with present concepts of disturbed pulmonary physiology in those states. Emphasis is placed on improving fluoroscopic and roentgenographic studies of chest physiology to improve present methods of estimating the extent of pulmonary disability. The most important chapters deal with the history of pneumoconiosis, types of pneumoconiosis, pathogenesis, and the classification of the roentgenologic manifestations. This monograph should be of value not only to radiologists but also to internists, chest physicians, industrial physicians, industrial hygienists, pulmonary physiologists, bronchologists, industrial engineers, thoracic surgeons, and medical students.

Radiation Biology and Medicine: Selected Reviews in the Life Sciences. Edited by Walter D. Claus. Prepared for United States Atomic Energy Commission. Cloth. $11.50. Pp. 944, with illustrations. Addison-Wesley Publishing Company, Inc., Reading, Mass., 1958.

The output of research publications on ionizing radiation since the advent of the atomic bomb and establishment of nuclear reactors has been truly staggering. In addition to thousands of individual journal articles and reports from governmental agencies, many volumes of symposiums on specialized topics have appeared. This book serves a real function in bringing together in a series of reviews an up-to-date account of the impact of atomic energy on such diverse fields as genetics, physiology, agriculture, and medicine, to name but a few, as well as on such varied but related problems as growth and aging, ecology, and bioeconomics. The editor makes it clear at the outset that the nature of the task has forced selection of only certain areas for review and, furthermore, that the scope of presentation has been limited essentially to work performed or in progress in the United States. Despite this fact, the coverage is excellent, and the 33 chapter headings have been selected with care. The authors present their specialties with competence and have written concisely and authoritatively, yet without "writing down" to their varied audience. Those who wish to refer directly to source material will welcome the extensive bibliographies accompanying each topic. The reviews of the medical uses of atomic radiation point up the wide application of radioisotopes today, as well as the development of accelerators and the nuclear reactor itself as a device for medical therapy and diagnosis. Already some 350 devices using radioactive cobalt (Co^{60}) as a teletherapeutic source are in use. The problems of instrumentation and dosimetry are well covered, and scanning technique, probably the most outstanding development in medical instrumentation within the past few years, comes in for its share of attention. In these days of international hysteria and debate, the basic material presented in this book should go far in providing factual information for the intelligent reader concerned about radiation hazards.

Reversible Renal Insufficiency: Diagnosis and Treatment. By Donald H. Atlas, M.D., Ph.D., F.A.C.P., Associate Professor of Medicine, Northwestern University School of Medicine, Chicago, and Peter Gaberman, M.D. Cloth. $7. Pp. 233, with 19 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2, 1958.

The authors' experiences at the Cook County and Mt. Sinai hospitals in Chicago and a thorough review of the literature on the pathology, pathological physiology, and therapy of acute renal failure, with oliguria and uremia, have served as the basis for this monograph. More space is devoted to a review of conditions associated with elevated plasma calcium levels than to all forms of therapy for acute and chronic renal failure (50 compared to 40 pages). The review of hyperparathyroidism, "milk-alkali" syndrome, sarcoidosis simulating hyperparathyroidism, and other conditions associated with hypercalcemia is well worth study, as are the sections on lupus, gouty kidney, and other renal disorders. This can be recommended as a sound guide to the management of the oliguric and polyuric phases of acute renal damage.

Physiology of Exercise. By Laurence E. Morehouse, Ph.D., F.A.C.S.M., Professor of Physical Education, University of California at Los Angeles, and Augustus T. Miller Jr., Ph.D., M.D., Professor of Physiology, University of North Carolina Medical School, Chapel Hill. Third edition. Cloth. $4.75. Pp. 349, with 40 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1959.

This book constitutes a compact summary of material conventionally taught in connection with athletics. The opening chapters contain some of the classic fundamental facts about the histology, biochemistry, and physiology of voluntary muscles, with some of the more recent findings in these fields. Subsequent chapters are concerned with skills, muscular strength and hypertrophy, stress and endurance, energy requirements and efficiency, fatigue and recovery, training, nutrition, medical aspects of exercise, and physical fitness. Each chapter is followed by a bibliography, which is essential because of the brevity of many parts of the text. The book ends with a glossary, a convenient table of conversion factors for weights and measures, and a good index.

The scientific value of this book could have been greatly increased if advantage had been taken of the results of research in fields other than athletics, by greater concreteness in the discussions of the neurophysiology of muscular tone, by more frequent use of the precise vocabulary of kinesiology, and by eliminating some unfortunate terms, such as linear, lateral, eccentric, and concentric, inherited from the uncritical past. The statement (page 77) that "an attempt to contract the biceps voluntarily will not produce the movement" ignores the existence of the art of muscle control. The statement (page 253) that swimming develops "long" muscles is not borne out by the illustrations showing four men, one a swimmer, whose extremities are clearly of the same absolute and relative length. In most respects, however, the book deserves commendation as a compendium of scientifically verified facts of importance in physical education.

Lesions of the Lower Bowel. By Raymond J. Jackman, M.D., M.S., Associate Professor of Proctology, Mayo Foundation, Graduate School, University of Minnesota, Rochester. Cloth. $15.50. Pp. 347, with 131 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This is an excellent volume. The color plates depicting polyps, carcinomas, the lesions characteristic of ulcerative colitis, and other frequently seen lesions (as well as a few rare ones) are superb. This monograph is not a book on proctology or proctologic surgery per se, and apparently it is not intended to replace such a book in the physician's library. The style is rather that of a diagnostic study, dealing with the methods of performing proctologic examinations and the recognition of lesions most frequently encountered. This idea has been carried out clearly, concisely, and authoritatively.

The chapter on the technique of proctoscopy is well done. Step by step the reader is instructed in indications, preparation of the patient, positions, and the actual conduct of anoscopy and proctosigmoidscopy. The accompanying illustrations should clear up many misunderstandings held by beginners in these procedures. The technique of transrectal needle biopsy as it applies specifically to prostatic biopsy is included, surprisingly. Fifty-six black-and-white illustrations and a color atlas of 75 plates add a great deal to its usefulness. There are 28 chapters, each indexed with a subject-matter heading for easy reference. A wide diversity of medical men—the general practitioner, the gastroenterologist, the proctologist, and the general surgeon—will find this book a valuable addition to their working libraries.

QUESTIONS AND ANSWERS

SPEED OF TRANSFUSION

To the Editor:—*What is considered the maximum rate of administration of whole blood during transfusion?* *H. E. Rendel, M.D., Mexico, Ind.*

Answer.—The maximum rate of administration of whole blood during transfusion is considered to be about 250 ml. per minute. In actual practice the maximum rate is related to the amount of blood that can be forced through a 15-gauge needle into an accommodating vein or veins. Several problems may result from the rapid administration of a large amount of whole blood. The first is the remote possibility of citrate intoxication, although this rarely, if ever, happens. A second complication that can follow the rapid administration of whole blood in massive amounts is thrombocytopenia with serious clotting disturbance. This has occurred clinically and can be produced experimentally. Overloading the circulation can result in pulmonary edema. Good clinical judgment is always necessary in deciding how much blood should be given in what period of time.

DIAGNOSIS OF RENAL TUBERCULOSIS

To the Editor:—*In this area, there is a difference of opinion as to the best method of identifying tuberculous organisms in the urine. Staff members at one hospital insist that urine cultures provide the most consistent results. At another hospital, they believe that urine cultures are not as effective as guinea pig inoculation. Should not all methods, namely, acid-fast stain, culture, and guinea pig inoculation, be used whenever possible? There is also a difference of opinion regarding the collection of the urine sample. Some believe that only a 24-hour specimen provides any degree of accuracy, while others accept a morning specimen.*

Carl K. Pearlman, M.D., Santa Ana, Calif.

Answer.—No dependence should be placed for diagnosis, especially for initial diagnosis, solely on microscopic examination of the urine, especially voided urine, because of the constant presence about the external urogenital orifice of saprophytic, acid-fast bacilli microscopically indistinguishable from Mycobacterium tuberculosis. These deceptive saprophytes are only with difficulty excluded from urine specimens, even from catheterized specimens. Urine for bacteriological examination should be obtained by means of a sterile catheter to avoid the inevitable contamination of voided specimens. If voided urine is used, 24-hour specimens are preferable because they are more likely to contain tubercle bacilli than a single voided or catheterized specimen, since the bacilli are often shed intermittently. However, 24-hour specimens are usually heavily contaminated unless refrigerated and require decontamination with consequent loss of some of the tubercle bacilli.

The controversy over culture vs. guinea pig inoculation continues in the absence of general acceptance of a culture procedure. The number of cultures, decontamination, and concentration methods presented in the literature testifies to general dissatisfaction with (but not necessarily to inferiority of) existing procedures. A strictly fair comparison between culture methods and guinea pig inoculation requires that the same amount of the same material be used to inoculate, as nearly simultaneously as possible, guinea pig and cultures in a sufficiently large number of cases to yield a statistically significant result. The patients selected should be those known to be shedding tubercle bacilli in numbers sufficiently small to test the sensitivity of each method, or else the comparisons should be based on such quantitative data as colony counts and rapidity of growth. It is also essential that culture methods be carried out exactly as recommended by their sponsors. Such studies are rare and, with regard to urine, virtually nonexistent. In too many studies of this sort, human and other variables, some known and some unknown, seem to have played a significant role.

There are now probably a dozen or more culture methods which, properly handled, yield diagnostic results as reliable as, and often more rapidly than, guinea pig inoculation. Discussions of these may be found in the literature. In any case, the identity and virulence of any acid-fast organism isolated in pure culture from urine or other contaminated material (such as sputum) must, at least for primary diagnosis, be verified by guinea pig inoculation. Additional physiological tests other than, or in addition to, guinea pig inoculation may be required in the case of some of the so-called atypical acid-fast bacilli recently recognized as possibly involved in tuberculosis-like infections. The use of guinea-pig inoculation alone would fail to detect a number of these atypical strains. Furthermore, pure cultures are desirable for sensitivity testing.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

The more methods that are used in any diagnostic test, especially in biological diagnostic tests such as cultural procedures, the more likely is a reliable result to be obtained (assuming minimal probability of obtaining a positive result). For example, the use of cultures and guinea pig inoculation together is more likely to give a dependable result in a minimal time than the use of either alone. The inoculation of 10 culture tubes is preferable to the inoculation of 1. In short, the wider the net, the more the fish. So far as procedures are concerned no specific recommendation need be made, but it may be said that, for urine, centrifugation of the specimen for 30 minutes at 4,500 rpm is necessary. If there is no flocculation or sediment a small amount of flocculating agent, such as ferric chloride, in urine made slightly alkaline with sodium bicarbonate, is advisable to gather the bacilli and sediment them. If the sediment is not heavily contaminated it may be used to inoculate, directly, slants of some medium such as the Holm-Jensen-Lowenstein medium, the Frobisher-Petragnani medium, or one of the later-devised blood or egg mediums. Contamination may be controlled by adding penicillin and cycloheximide to the culture medium. If heavily contaminated, preliminary decontamination with sodium hydroxide or sulfuric acid may be used, as for sputum, but these are toxic to M. tuberculosis and are to be avoided in favor of the antibiotics.

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CORNEAL HERPES SIMPLEX

To the Editor:—*A patient has had recurrent dendritic ulcer of the right cornea for five years. Recurrences are two to four weeks apart, and each attack has left the cornea partially denuded and has caused an irregular surface. Attacks last one or two weeks. Several physicians have recommended a corneal transplant as a means of preventing future ulcerations and to improve the present vision (20/400 in this eye). About one-half of the corneal surface has been affected. X-rays of the sinuses revealed a mild pansinusitis, and in July the ethmoid and sphenoid sinuses were operated on and the nasal septum was straightened. Autogenous vaccine was prepared and is still being given. The patient has taken vitamin B complex daily for the past five years, eats well, feels well, and has no chronic inflammatory lesion of any kind. The eye has been cauterized at least 20 times with iodine; the entire cornea has been scraped about three times. Every known ophthalmic ointment has been used, and all eventually caused irritation and had to be replaced by a milder preparation; 20 cc. of immune serum globulin has been injected intramuscularly on two occasions one month apart. Also, 20 smallpox vaccinations were administered twice a week. Large amounts of vitamin C are taken daily. It was recommended that, after subsidence of each acute phase, an ophthalmic ointment or solution be given twice a day, but since this has not prevented a recurrence of further ulcers all medicaments have been withdrawn. What further steps can be taken to stop the attacks? Is any research being done at present for such a condition and, if so, where? Have any ophthalmologists in the United States had a number of such cases, and were they successful in treating such a stubborn case? Would the use of contact lenses improve the vision, or would they further damage the cornea or excite an attack? Are sufficient statistics available to indicate or warrant transplantation in this case?* *M.D., New Jersey.*

Answer.—In the past 10 years there has been a marked increase in the frequency of chronic herpetic corneal ulcers, especially of those that lead to perforation. This is attributed to the widespread use of corticosteroids and antibiotics in the treatment of herpes simplex infections. The herpes simplex virus is one of the smallest known and is not affected by topical or systemic medication. Recurrences are brought about by multiplication of the virus within the tissues because of reduced local tissue immunity. They may be associated with upper respiratory infections, fever, menstruation, and minor ocular trauma, but for the most part no cause can be found. The mainstay of treatment has been destruction of the cells containing the virus with iodine, ether, or similar chemical cautery. As the inquiry indicates, many medicaments have been recommended to prevent recurrences and these are frequently without value.

Much research is being carried out on virus infections of the eye. The current status of these studies is synopsized in the Symposium on Viral Keratoconjunctivitis (*Am. J. Ophth.* 43:3 [part 2], 1957). Many ophthalmologists in the United States have seen a large number of patients with corneal herpes simplex, but because of the nature of the disease no particular method of therapy is consistently successful. A contact lens will improve vision only if the visual diminution results from an irregularity of the cornea. Generally, a contact lens is contraindicated in an eye in which herpes simplex infections recur frequently.

Therapeutic lamellar grafting is indicated in patients with chronic superficial ulcers that fail to heal after two or three months' treatment; in those with much deeper, more extensive ulcers that fail to respond in two or three months to a variety of treatments; to prevent frequent recurrences of dendritic ulcers; and in patients with chronic disciform ulcers that have perforated. Contraindications to lamellar keratoplasty are secondary infection by bacteria or fungi, glaucoma, and iridocyclitis. Lamellar keratoplasty has been performed in a number of patients with corneal herpes simplex. Frequently a penetrating graft is necessary as a secondary procedure to improve vision. The purpose of the therapeutic lamellar graft is to remove all of the diseased corneal tissue containing the virus. Since only a portion of the cornea is removed and the globe is not entered, the operation is not as technically difficult as a penetrating keratoplasty. It may frequently be associated with a gratifying improvement in vision. With a history of recurrent infections over a period of five years, this would seem to be an ideal case for corneal transplant, as suggested by the physicians who have already seen this patient.

BLOOD PRESSURE TRACINGS

To the Editor:—*Has anything practical and inexpensive been developed by which blood pressure may be graphically recorded in the office, thus removing the human element in its accurate interpretation? Do the occasional relatively wide variations in blood pressure readings recorded by different "competent" physicians or even by the same observer on repeated examinations represent true labile changes?* *M.D., California.*

Answer.—No practical, simple, and inexpensive instrument is available for graphically recording blood pressure in the office. The techniques used in physiological and crime detection laboratories are complicated and delicate. Furthermore, these instruments do not indicate precisely the level of diastolic pressure, concerning which there is widespread lack of unanimity even with the auditory method. The wide variations in observed blood pressure readings under accurately controlled conditions do represent actual fluctuations in pressure, but this fact need not be ominous or lead to concern. In the absence of pheochromocytoma, wide and rapid fluctuations are commonly seen as the result of the state of mind—rage or fear in extreme instances, concern, apprehension, a bad day or night, the novelty of coming to a strange physician, or where a momentous decision is to be expected. A man who has been examined for life insurance may be somewhat apprehensive. His pulse is rapid and his blood pressure elevated, so either he is rejected or his premium is increased. When he is seen by the family physician or a consultant who gains his confidence, his pressure is repeatedly found to be normal. One can observe a rapid fall in pressures as the patient's mind is directed from the realization that the pressure is being taken, and often it can be observed to rise as he again becomes aware of the procedure. No matter how satisfactory and how frequently this fall to normal may be observed in the office of a neutral observer, the pressure will invariably be elevated when he returns to the insurance examiner. Similar reactions are seen frequently in women referred for a gynecological examination and, in World War II, in young healthy men examined for officers' training. The above facts are the basis for the sedation test, in which the subject is given a relatively large dose of a sedative or tranquilizer, after which serial readings are taken every half hour for five or six periods. This may be considered a legitimate procedure in hyperreactors if the examining physician is informed of the program and is aware that no true blood pressure reducing or vasodilating preparation is being used. Thus, these fluctuating readings represent actual variations in levels of pressure, but the interpretations of these changes should be made with caution and after ascertaining the facts and behavior behind the changes.

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ERYSIPELAS AND CANCER

To the Editor:—*Recently, a lawyer asked about an article which advocated the use of erysipelas in the treatment of advanced carcinomatosis. The lawyer's secretary has generalized carcinomatosis, and he would like to know if she could be benefited by this treatment. Where and by whom is the experimental work on this form of treatment being done?* *A. A. Fink, M.D., Topeka, Kan.*

Answer.—The observation that in one patient who had been operated on five times for sarcoma there was no recurrence after two attacks of erysipelas prompted the late Dr. W. B. Coley to study the effects of induced streptococcic infections on tumors. Difficulties encountered included patient immunity and occasional death from infection. Heating or filtration appeared to destroy the effectiveness of the culture. Eventually, a mixture of toxins from erysipelas producing streptococci and Serratia marcescens came to be known as Coley's toxin. This material received extensive trial. All but a few preparations were weak and variable, but there are a number of reported tumor-free survivals of 20 to more than 40 years' duration. A review of the influence of bacterial infection and of bacterial products (Coley's toxin) on malignant tumors in man has been made by Nauts and associates (*Acta med. scandinav.* [supp. 276] 145:1, 1953). Unfortunately, it is impossible to determine the percentage of objective remissions achieved from the available data. The effectiveness of this form of therapy appears to be related to the production of a severe local inflammation augmented by a systemic febrile reaction. Daily injections for many months, sometimes interspersed with short rest periods, are required. It is necessary to provide means for evacuation of large quantities of necrotic tumor tissue to prevent toxemia from absorption. A more recent extension of this work has been the use of purified polysaccharides from bacterial cultures such as S. marcescens, but the reported results from such therapy are not impressive.

REACTION TO CHRYSOTHERAPY

To the Editor:—*A patient with rheumatoid arthritis received an initial injection of 25 mg. of gold sodium thiomalate. Twenty-four hours later he experienced swelling and itching of the scrotum and lower lip. The only other drug taken concurrently was dextropropoxyphene (two capsules every three hours for two doses). The literature concerning toxic reactions to gold mentioned pruritus and dermatitis but not an immediate urticarial reaction. Could the gold have caused this reaction? Paul Gerber, M.D., Philadelphia.*

Answer.—Immediate allergic reactions to the administration of gold, while rare, are not unknown. Either this or the other medicament taken concurrently could have been the precipitating factor in this patient. Probably 10% or less of patients will note an acute exacerbation of rheumatic symptoms within 24 to 48 hours after the administration of gold, and this is generally considered to be an allergic manifestation. It is not an indication for discontinuing treatment but rather for decreasing the size of the dosage. If the case that forms the basis of this inquiry is one in which gold is indicated, a single dose of 1 mg. of gold sodium thiomalate could be given intramuscularly at a future date, and if no untoward reaction occurred to this dose an injection of 5 mg. could be given one week later. If no reaction is noted the dose could then be increased 5 mg. each week to a maintenance dose of 25 mg. The appearance of allergic manifestation after the administration of any of these injections would be a sign for discontinuance of this type of therapy. Because of the potential toxicity of chrysotherapy, it seems wise when instituting such treatment in any patient with rheumatoid arthritis to use only 5 or, at most, 10 mg. of gold as an initial dose and to increase to the maintenance dose of 25 or 50 mg. by increments of not over 10 mg. per week.

BOILED PEANUTS FOR DIARRHEA

To the Editor:—*A 34-year-old woman who had had intermittent abdominal pain for four years had an exploratory laparotomy in November, 1956. At that time a terminal ileitis involving the distal 10 in. of the ileum was found. The terminal 2 ft. of ileum were resected and an end-to-side ileoascending colostomy was performed after closure of the ileocecal opening by inversion. There were no skip areas, and no other abdominal lesions were noted. The pathological report showed chronic granulomatous inflammation of the terminal ileum compatible with regional ileitis. After operation the patient recovered, but diarrhea has persisted and has not responded to ordinary therapy. In February, 1957, a complete gastrointestinal examination was done with negative findings and she was given prednisone; this therapy was continued throughout the year with the patient gradually returning to normal weight and vigor. Therapy was stopped in March, 1958, but she continued to have six to eight stools a day with mucus but no blood. The patient has found that if she consumes a pint or more of boiled peanuts daily the symptoms are controlled. This does not happen with folic acid, vitamin* B_{12}, *antispasmodics, pancreatin, or any other dietary measure. On several occasions when the peanuts were not taken the diarrhea returned, only to disappear again with their ingestion. Please give information that would lead to some specific form of therapy.*

C. H. Richardson Jr., M.D., Macon, Ga.

Answer.—The control of diarrhea by boiled peanuts in a patient who has had a resection of the distal ileum is a most interesting observation. This consultant knows of no explanation for this, but peanuts and other nuts contain a number of constituents that have physiological or pharmacological action. Several glycosides that have a goitrogenic action have been isolated from edible nuts (*J. Nutrition* 66:291, 1958). The outer red skin-covering of certain nuts has been found to contain anthocyanins and tannins. Such compounds might conceivably decrease the activity of the intestinal mucosa. An alcohol-soluble material has been found in peanuts which may have an influence on blood coagulation in hemophilia. Further study of the effect of boiled peanuts in the therapy of diarrhea appears to be warranted.

METABOLIC RATE IN AN AMPUTEE

To the Editor:—*Please give advice on the determination of basal metabolic rate in a patient suspected of having hypothyroidism. The difficulty lies in the fact that this patient has had both legs amputated at midthigh because of gangrene, complicating diabetes mellitus. The problem is the determination of the patient's body surface. Her blood cholesterol level is within normal limits. The protein-bound iodine and radioactive iodine uptake tests are not locally available.*

Leo Lewin, M.D., Mount Arlington, N. J.

Answer.—The true surface area of this patient can be determined with reasonable accuracy by making a series of linear measurements of body parts and applying the "linear formula" as described by DuBois and DuBois (*Arch. Int. Med.* 15:868, 1915). Unfortunately, this will not solve the problem. Normal standards for calories per square meter (or liter of body water) are entirely empirical, i. e., they are merely average values observed in healthy, intact persons. They are not applicable to amputees because the various body parts are far from uniform in terms of calories per square meter. For example, the bilateral, midthigh amputation probably reduced this patient's surface area by about 30% but her basal heat production by less than 10%. The simplest procedure is to use the patient's preamputation height and weight in calculating a basal metabolic rate in the usual fashion; then, in order to make allowance for a 10% reduction in calorie output due to the amputation, set the "normal range" for this patient at —25% to +5%. In view of the uncertainty in this procedure and because of the propriety of conservative management of hypothyroidism in the presence of diabetes, a protein-bound iodine level determination would be desirable. This can be done on a mailed plasma sample.

USE OF THIOPENTAL IN LABOR

To the Editor:—*How soon does thiopental reach the infant circulation if used in cesarean section? What are its advantages and hazards?*

D. D. Dieter, M.D., Eustis, Fla.

Answer.—On the basis of work by Crawford (*Brit. J. Anaesth.* 28:146, 1956) and others, it is generally believed that thiopental, if used for cesarean section, passes immediately from the mother to the fetus. While certain advantages are associated with the use of thiopental for cesarean section (pleasant, easy induction of anesthesia, control of eclamptic convulsions, or decreased incidence of postanesthetic vomiting), definite hazards are involved. These include respiratory depression of mother and, especially, of the infant and increased possibility of severe respiratory spasm if the mother has recently ingested food. While the drug is not contraindicated for use during cesarean section, it should be given only with full appreciation of the risks involved.

HYPERKERATOSIS

To the Editor:—*An 11-year-old boy developed a thick scaling cracking of the palms of the hands and soles of the feet four years ago. This resembles ichthyosis but is limited to the palms and soles. The condition has remissions and exacerbations which occur every three or four months. The soles of the feet have been relatively free from the scaling but appear dry. At the times of exacerbation of the condition the nails become brittle and break easily. The boy's general health has remained good. Many treatments have been tried with little success. In general, the most successful has been applying simple softening ointments to the skin and waiting from two to three weeks for the natural remission. Would this condition suggest a deficiency state? What tests and treatments might be beneficial?*

Dwight E. Conklin, M.D., Oakland, Iowa.

Answer.—Hyperkeratosis of the palms and soles (keratosis palmaris et plantaris) usually begins in childhood. Most cases are familial and in such patients no deficiency state has ever been demonstrated. Red, thickened, scaly palms and soles have been described as a manifestation of psoriasis and of pityriasis rubra pilaris. They may result also from mycotic infection, especially with Trichophyton rubrum. Numerous repeated examinations of the scales under potassium hydroxide and cultures must be done to exclude T. rubrum, particularly in view of the nail changes described in this case. In keratosis palmaris et plantaris bland lubricants and the avoidance of irritants provides comfort; a 1 or 2% solution of salicylic acid may be incorporated to promote peeling. No internal therapy (vitamin A, thyroid, or gelatin) has proved to be of value consistently. The prognosis should be guarded. Generally, patients retain the condition throughout life.

HAZARDS OF METALLIC PAINT

To the Editor:—*Is there a safe process by which a person can be covered with bronze or metallic paint?* *John H. Calvert, M.D., Pierce, Neb.*

Answer.—No form of this practice may be regarded as proper. At best, all such paints constitute a physiological insult to the skin. At present, real metal powders ordinarily have given way to plastic powders made to resemble metals or to fluoresce. Vehicles of the varnish type have disappeared, and corn syrup and glycerine are currently in favor. These agents do not dry the skin and may be readily washed from the body.

COMPOSITION OF COMEDONES

To the Editor:—*What is the composition of comedones? Has any work shown whether they are related to elevated blood cholesterol level, lipids, or androgens? Have there been any surveys of incidence of acne among different races and different dietary groups?*

G. H. Hoehn, M.D., San Gabriel, Calif.

Answer.—Some information, though fragmentary, regarding each of these questions is contained in a publication by Washburn and Liese (*J. Lab. & Clin. Med.* 41:199, 1953). These authors also found that the cholesterol content of sebum was higher than normal in an adult with testicular insufficiency. The sebum cholesterol level was elevated to that usually found prior to puberty, and it dropped after testosterone therapy. Investigations of the composition of comedones are scanty, and further studies might be valuable. There are, however, several reliable reports on the composition of sebum in acne vulgaris. A concise review was published recently by Wheatley (*Practitioner* 180: 580, 1958). Kile and co-workers (*Arch. Dermat. & Syph.* 61:792, 1950) did not find any significant deviation of the sebum composition in skin areas affected by acne from that in unaffected areas of patients with acne or of normal persons. Dubovyi (*Vestnik Vener. Dermat.*, no. 2, p. 22, 1955), however, demonstrated a higher ketosteroid percentage in subjects with acne, and Wheatley's recent studies are highly suggestive of a lower concentration of unsaturated fatty acids. As pointed out by Rothman and Schaaf (*Handb. d. Haut-u. Geschlechtskr.* 1:161, 1929) and again by Rothman in his textbook "Physiology and Biochemistry of the Skin" (Chicago, University of Chicago Press, 1954), ingestion of large amounts of cholesterol with the food can increase the cholesterol concentration in sebum.

TRACTION FOR WHIPLASH INJURIES

To the Editor:—*How useful is intermittent traction in the treatment of whiplash injuries or when pelvic traction is desired? Are the motorized traction apparatuses good for this purpose? If so, what types are best, and where may they be obtained?*

Delbert L. Warwick, M.D., Costa Mesa, Calif.

Answer.—The exact pathogenesis of whiplash injuries has not been determined. The acute episode probably is a sprain, with tearing of certain of the ligaments in the neck. There may be disturbances in the facet joints, as well as the lateral vertebral joints. Herniation of the nucleus pulposus also may occur as a result of whiplash injury. In none of these circumstances, with the possible exception of herniation, can benefit be expected from traction. Cervical traction probably has no justification in the treatment of so-called whiplash injuries. This applies during the acute period and for several weeks after the injury. Degenerative changes may result from whiplash injuries, with narrowing of the intervertebral disks, formation of hypertrophic spurs, and, sometimes, appearance of radicular symptoms and signs or both. During this phase cervical traction may be tried for its effect. If helpful, it may be continued. It is not clear whether the questioner means to use pelvic traction in treatment of whiplash injury. There seems to be no rationale for its use in this condition. It is used as part of the conservative management of lumbar disk affections. Motorized traction apparatuses are helpful in treating certain cervical syndromes, chiefly those due to degenerative disease, but the usual whiplash injury is not in this category.

FILLINGS AND LEUKOPLAKIA

To the Editor:—*Is there any evidence that mercury amalgam and gold fillings in the same mouth predispose to the formation of leukoplakia?* *M.D., West Virginia.*

Answer.—There is no definitive evidence to support the concept that metallic fillings of varying electrical potentials predispose to oral leukoplakia. When an electrical force is produced under these circumstances it is on an intermittent basis and in a limited time ceases to repeat itself. Thus, if the electrical force can be considered trauma, it is not a chronic irritation. Patients may be aware of a salty taste which they attribute to the opposing metallic fillings, but this is often erroneous.

SCHMORL'S NODULES

To the Editor:—*A patient who died of multiple myeloma had showed Schmorl's nodules in an x-ray film about 11 years earlier. Should a patient presenting such nodules receive periodic bone surveys for several years?*

M.D., California.

Answer.—Schmorl's nodules, an acquired process, represent extrusion of a portion of the nucleus pulposus through the cartilaginous plate of the intervertebral disk into the body of the vertebra. They accompany the condition occurring in adolescents variously called juvenile kyphosis, Scheuermann's disease, or vertebral epiphysitis. They are also commonly found late in life and have no clinical significance except that their presence indicates some degeneration of the intervertebral disk. Periodic bone surveys are not indicated. The nodules have no relationship to and should not be confused with myeloma.

REJUVENATION

To the Editor:—*Is there any contraindication to the administration of gonadotropins to elderly men for possible rejuvenation or stimulation of their potency? Many advertisements recommend such treatment. How effective have these agents been for these purposes? What are the upper limits of safety for the continued use of these drugs?* *M.D., Missouri.*

Answer.—There are no specific agents for the purpose of rejuvenation, but there are few, if any, contraindications to the administration of gonadotropins in small amounts, such as 0.167 mg. of estrone plus 1.67 mg. of methyltestosterone in a capsule given three times a day. However, the activity of prostatic malignancy is affected by the intensity of androgenic stimulation.

CLIMATE AND RHEUMATOID ARTHRITIS

To the Editor:—*A 17-year-old girl has had severe rheumatoid arthritis for about a year. At present she is much improved. She is now making plans for college. Would she be better in Denver than here in Minnesota?* *M.D., Minnesota.*

Answer.—This consultant knows of no scientific evidence to indicate that climate is an important factor in rheumatoid arthritis. Some patients with rheumatoid arthritis feel better in a warm, dry climate, and some feel better in a relatively dry climate of higher altitude. In any climate, good treatment for the disease needs to be carried out in order to obtain the best results in controlling the disease. Since the patient has improved in her own environment, she would probably get along well in college either in Minnesota or Colorado, providing she continued to get good medical care.

ANTIBIOTIC COMBINATIONS

To the Editor:—*Is it ever practical to use both penicillin and a tetracycline simultaneously in the treatment of an ordinary and uncomplicated infection, such as otitis media or acute tonsillitis?*

M. A. Cornwall, M.D., Hudson, Wis.

Answer.—Combined antibiotic therapy may be used in patients with mixed infection to prevent the emergence of resistant bacterial mutants and for additive or synergistic effects against relatively resistant organisms. In ordinary uncomplicated otitis media or acute tonsillitis, it is needless, impractical, and illogical to use penicillin and a tetracycline simultaneously.

WOLFF-PARKINSON-WHITE SYNDROME

To the Editor:—*In the Wolff-Parkinson-White syndrome, during episodes of tachycardia, does the abnormal conduction pathway revert to normal, giving a QRS complex of normal measurements and form?*

Irving Berlin, M.D., Newport News, Va.

Answer.—During the episode of tachycardia, the QRS complex usually is of normal form and duration.

PROPHYLACTIC SURGERY IN CANCER

To the Editor:—*The answer to the question on prophylactic surgery in cancer, which appeared in* The Journal, *Jan. 10, 1959, page 183, needs some elaboration. The question is not whether an operation should be performed but whether it would be justifiable for three sisters, aged 38 to 42, to have prophylactic bilateral simple mastectomy when each of four older sisters has died from metastasis of breast cancer, within less than five years after radical mastectomy, at ages between 45 and 55 years. The answer to this seems to be an unequivocal "It would be justifiable." Whether it should be done is a matter of personal opinion and depends on such factors as general health, emotional make-up, and marital status.*

Although mastectomy is a traumatic experience for a woman, as the answer states, awareness of the fact that four sisters developed and died of cancer of the breast in the age period a woman is entering is probably at least as traumatic psychologically as the mastectomy and possibly more so. Since all four sisters died within five years, although the lesions had been found early, one can assume that they had unusually invasive malignancies and the same type would conceivably develop in the remaining sisters. This should be one more reason for a prophylactic operation. Where the psychological impact of mastectomy may be too damaging, it may be advisable to excise the glandular tissue of the breasts without removal of skin and nipple and to replace it by implantation of some foreign material.

Hans L. Popper, M.D.
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The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*In the opinion of this consultant, prophylactic mastectomy under the stated circumstances is not justifiable. Furthermore, the foreign material generally used for the replacement of the normal gland structure is potentially carcinogenic, and such a practice should be mentioned only to be condemned.*

ELECTROSHOCK THERAPY

To the Editor:—*I would like to refer readers of* The Journal *to* Time *magazine, Jan. 26, 1959, page 23, and the article about "Plaintiff's Counsel," which tells the story of the "King of Torts," Melvin M. Belli, whose pet peeve is doctors and who presently is performing in Columbus, Ohio. In* The Journal *for Jan. 24, 1959, page 419, a question is asked about ventricular fibrillation as a complication of electroshock treatment. In answer to the question: "Does the rapidity of injection of succinylcholine have any bearing on the incidence of ventricular fibrillation?" the second consultant very properly adds that the management of circulatory arrest in the course of electroshock therapy depends, as in other such cardiac emergencies, on establishing as quickly as possible the type of abnormal mechanism, whether rapid ectopic impulse formation or cardiac standstill. Here the consultant goes out of his way to make a statement which I predict will warm the heart of Mr. Belli; he says, "Such a distinction is greatly aided by the monitoring of cardiac events on a cardioscope, which should be part of the routine equipment in any setup for shock therapy."*

How can a clinical psychiatrist, even in a hospital, afford to include cardioscopy as a routine measure for shock therapy? I would question whether 1% of the treatments in the United States are given with a cardioscope to monitor the cardiac events. Yet this statement would lead one to believe that without the cardioscope the physician has not taken reasonable precautions, and I would predict that this statement will be used to place in jeopardy the practice of well-qualified psychiatrists who have given thousands of patients electroshock treatment without even suspecting that a cardioscope should be "routine equipment."

I believe that statements appearing in the Questions and Answers section should be carefully read for possible medicolegal angles, particularly when the consultant is surrounded by the unlimited services of a large medical center and is not familiar with the conditions under which the average physician attempts to carry on the practice of medicine.

George T. Harding, M.D.
445 E. Granville Rd.
Worthington, Ohio.

The above comment was referred to a consultant, and his reply follows.—Ed.

To the Editor:—*Doctor Harding states that less than 1% of the shock therapy treatments given in the United States are given with a cardioscope to monitor the cardiac events. He is apparently concerned over the fact that, inasmuch as the cardioscope is not routinely used, the result may be to aid malpractice attorneys in planning cases against physicians where a cardioscope might have avoided a bad result from shock therapy. The fact that a consultant may recommend the use of a cardioscope would not establish negligence on the part of the physician who failed to use such equipment unless the plaintiff could establish that the use of such equipment was routine and standard. If less than 1% of the treatments in this country are given with a cardioscope to monitor the cardiac events, a plaintiff's lawyer would not be able to establish negligence because of the failure to use such equipment. This consultant does not believe that a medical consultant should be burdened with medicolegal implications where his recommendations involve matters relating to better medical care nor that there is any need to review routinely strictly medical matters for medicolegal implications. Although it is felt that physicians should be aware of their legal responsibilities in the practice of medicine, it seems that some practitioners have been oversold on the idea.*

RECURRENT INFECTIOUS MONONUCLEOSIS

To the Editor:—*In the questions and answers section of* The Journal, *Dec. 27, 1958, page 2332, no specific case is cited in reply to an inquiry as to whether infectious mononucleosis has been reported to occur a second time in the same patient. I should like to call attention to a report by Paterson and Pinniger (Brit. M. J. 2:476, 1955) describing three attacks of infectious mononucleosis in a young man at the ages of 14, 18, and 21 years. The diagnosis was supported by laboratory evidence in each instance. This is a most unusual occurrence. A review of reported cases of recurrence by these authors disclosed only one other case in which the diagnosis was confirmed by the Paul-Bunnell reaction.*

Harry Wiener, M.D.
630 Flushing Ave.
Brooklyn 6, N. Y.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The difficulties in studying the recurrence of infectious mononucleosis are well illustrated in the paper by Paterson and Pinniger cited in the comment, since, even in the thoroughly investigated case reported, they were unable to secure the hematological findings or the results of the Paul-Bunnell test when the first two attacks occurred. They satisfied themselves,* *however, that at least the second attack—suffered while the patient was serving in the Royal Air Force—was genuine, as shown by laboratory tests. When he was sick at the age of 14, "he had symptoms of infectious mononucleosis [and] the white blood picture was said to be suggestive of the disease and the Paul-Bunnell test to be positive." In the second case mentioned in the comment, presumably the one reported by Rugg-Gunn* (Proc. Roy. Soc. Med. 47:759, *1954), the patient had the clinical findings of infectious mononucleosis at the age of 6 but hematological investigation was not done. Eight years later he again showed enlargement of the glands of the neck; blood examination was done, and the diagnosis of "glandular fever" was given. At the age of 20 he once more showed symptoms of the disease, and at that time both the differential counts and the Paul-Bunnell test confirmed the diagnosis. In the paper by Paterson and Pinniger, the findings of Bernstein in his review of the disease are cited. Of five cases of recurrence, in only one was the diagnosis confirmed during the second illness by the Paul-Bunnell test. Here the patient had initially an icteric type of illness, which was followed a year after recovery by an episode of glandular enlargement with fever. As the Paul-Bunnell test was not done on the first occasion, it seems that the possibility of this case being infectious hepatitis at that time cannot be entirely excluded. It appears, therefore, that the recurrence of infectious mononucleosis is rare, at least as judged by the cases reported in the medical literature.*

CELERY CONTACT DERMATITIS

To the Editor:—*In reading the answer to the question on celery contact dermatitis, which appeared in* The Journal, *Jan. 10, 1959, page 185, it occurred to me that there might be another explanation for this syndrome. This dermatitis, like that associated with parsnips* (Acta dermat.-venereol. 25:179, *1944), may be due to the presence of photodynamically active furocumarines in these plants. Members of the psoralen family are present in such substances as citrus oils and bergamot, the best known being methoxsalen or 8-methoxypsoralen, from Ammi majus L. Aside from the fact that workers at the University of Oregon School of Medicine have recently demonstrated significant amounts of psoralens in celery, the natural history of the dermatitis suggests contact with a photodynamic agent. The statement that "the harvesters were afflicted" would be true because these workers would also be exposed to ultraviolet energy. It is also stated that the eruption appeared "within 24 to 48 hours." A latent period of one to two days is usual after use of the psoralens. The eruption consisted of "erythema, edema, vesicles, and large bullae." This was presumed by the consultant to be on the hands, forearms, and perhaps the face and neck." These are precisely the areas either certainly or very likely to be exposed both to celery oil and to sunlight. Also, how better could one describe severe sunburn?*

In the light of these data, a rational, preventive approach may be recommended for trial. Psoralens augment the skin's response to ultraviolet energy and have no demonstrable topical activity in the absence of that energy. Field workers should be advised to avoid skin contact with the essential oil and direct solar exposure. Such measures as wearing sleeves rolled down and wearing gloves would help in two ways: contact with the plant would be minimized, and ultraviolet rays would be screened out. An extensive publication on psoralens and radiant energy (J. Invest. Dermat., *supp., Feb., 1959) should be consulted for further information on this fascinating subject.*

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The Upjohn Company
Kalamazoo, Mich.

NEURITIS OF RECURRENT LARYNGEAL NERVE

To the Editor:—*In response to a question and answer regarding neuritis of the recurrent laryngeal nerve, which appeared in* The Journal, *Dec. 27, 1958, page 2329, I noticed that the consultant failed to mention the possibility of laryngeal crises associated with tabes dorsalis (Fien and others,* Am. J. Syph. 36:201, *1952). The possibility of laryngeal crises associated with tabes dorsalis should be borne in mind in such a patient as that described in the question.*

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The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*Although the correspondent is correct in pointing out the possibility of laryngeal crises in tabes dorsalis, this is a rare occurrence and reference to it is encountered much more frequently in earlier medical literature than in recent years, probably because of the decreased incidence of central nervous system syphilis. Laryngeal findings in tabes are usually preceded or accompanied by other signs and symptoms of the disease. It was assumed from the initial query that the various diagnostic studies on the patient in question had included a thorough physical examination and complete laboratory tests.*

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TREATMENT OF PULMONARY EMPHYSEMA

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and
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The etiological diagnosis is of basic importance in patients with emphysema because the distinction between primary and secondary types decides the plan of treatment. The general aim of treatment is to keep the patient active; to preserve as much lung tissue as possible, and to maintain comfort. In primary emphysema, breathing exercises and such expectorants as potassium iodide are helpful, and in severe cases oxygen is indicated if used with due caution. But in secondary emphysema it may be necessary to use bronchodilators and steroids to combat underlying bronchial asthma, antibiotics to stop destructive infections, and other therapy directed at the original cause.

PULMONARY emphysema is a disease characterized pathologically by loss of elastic tissue and destruction of alveolar walls in the lung leading to the formation of enlarged air sacs. The physiological abnormalities are uneven distribution of inspired air, expiratory airway obstruction, loss of alveolar capillary surface available for diffusion, reduction in the vascular bed, and, eventually, pulmonary hypertension and cor pulmonale. For the purpose of this paper emphysema is classified as localized or generalized. The localized type of emphysema consists of one or more greatly enlarged alveoli with the rest of the lung normal. This probably is a congenital abnormality of one part of the lung. When cystic areas interfere with function by compressing normal lung tissue, they can be successfully removed. The generalized disease can be of unknown cause, or it can result from such disorders as bronchial asthma, bronchiectasis, tuberculosis, silicosis, and other types of chronic lung disease. Most of this discussion concerns the generalized form of the disease.

In the treatment of the patient with emphysema it is extremely important to establish the etiology of the emphysema. If it is secondary to bronchial asthma the treatment is primarily the treatment of bronchial asthma. Many physicians fail to make a clear distinction between bronchial asthma with emphysema and emphysema with chronic bronchitis. The disease in the patient with bronchial asthma and emphysema usually starts with attacks of paroxysmal dyspnea, frequently at night. The patient with primary emphysema early in his ill-

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Read before the Clinical Meeting of the American Medical Association, Minneapolis, Dec. 5, 1958.

ness has dyspnea only with exertion, so his sleep is not interrupted. The patient with bronchial asthma and emphysema may have rhinitis and nasal polyps, sinusitis, and eosinophilia. The patient with emphysema and chronic bronchitis usually does not. The chest roentgenogram in both is similar, showing hyperaeration. Pulmonary function tests may not make a distinction between the two disorders; the patient with primary asthma and secondary emphysema may show improvement in vital capacity, maximal breathing capacity, and maximal flow rates after the administration of epinephrine (Adrenalin), whereas the patient with primary emphysema has a minimal or slight response. Bates [1] has reported good results in making the differentiation on the basis of diffusion, which should be normal in patients with bronchial asthma and reduced in patients with emphysema. When the asthmatic patient develops secondary emphysema, however, this test loses its value in distinguishing between these two disorders. The patient with bronchial asthma responds well to steroid therapy, whereas the patient with primary emphysema responds poorly. We believe that good response to steroid therapy in patients with pulmonary emphysema is reported because of a poor distinction between the patient with bronchial asthma and emphysema and the patient with primary emphysema. Those with bronchial asthma almost invariably improve with steroid therapy.

Aims of Treatment

Let us direct our attention to treatment of the emphysema itself. In the patient with emphysema the primary aims of treatment are to keep the patient active, to preserve as much lung tissue as possible, and to maintain comfort. The main threat to the patient is further destruction of lung tissue by infection. Therefore, all respiratory infections should be treated vigorously for an adequate period of time. In each patient, efforts should be made to find the cause of the infection. Sputum and blood should be cultured. Antibiotic therapy must be directed toward eradicating the organism causing the disturbance. Satisfactory sensitivity tests are extremely important. While awaiting the culture report, we usually use the following plan: If the patient has fever we treat him with procaine penicillin G, 300,000 units given every 12 hours, on the theory that this may be a pneumococcus type of infection which will respond to penicillin. We assure ourselves that the patient is not sensitive to penicillin by asking him about previous reactions. If he is sensitive to penicillin, erythromycin is used as outlined below. If the patient has no fever but is coughing up purulent sputum, we usually start erythromycin therapy with a dosage of 250 to 500 mg. given four times a day. The rationale is that these infections are frequently staphylococcic in origin and may respond to this therapy. Antibiotic therapy should be given for at least 10 to 14 days if once started.

The next objective of treatment is to keep the patient active. Whenever possible we recommend that he continue his work. A job requiring extensive manual labor may be impossible. Attempts should be made to find a less taxing job. The patient should be urged to exert himself to the extent of his ability and told that shortness of breath acts as a warning sign and means the time to rest is at hand. He need not fear dyspnea, for in itself it is not harmful.

The next aim of therapy is to make the patient comfortable. One of the primary problems is to clear the tracheobronchial tree of thick, tenacious, sticky secretions. Benefit can be obtained with saturated solution of potassium iodide, given in a dose of 15 drops in a half glass of water three or four times a day. This drug seems to modify sputum, in an unknown manner, so as to make it easier for the patient to expectorate. It is the best type of cough medicine to give the patient with chronic emphysema. Cough mixtures containing codeine, morphine, or meperidine (Demerol) hydrochloride, which act by suppressing the cough mechanism, should be avoided. Meperidine, especially, dries secretions and increases the difficulty of clearing the tracheobronchial tree. Bronchodilators are of only limited value in the treatment of emphysema. The patient with emphysema has expiratory airway obstruction, but it is not usually caused by intraluminal obstruction or bronchiolar spasm but by a check-valve mechanism. Because of loss of elastic tissue, the airways are poorly supported. On forced expiration they collapse. When infection occurs, mucosal edema, congestion of blood vessels in the mucosa, and secretions within the lumen of the bronchioles obstruct the airway. Epinephrine and ephedrine constrict mucosal blood vessels and improve air flow. If bronchodilators are given, they should be given both locally and systemically. When the patient inspires, air flows to the areas in the lung with the best ventilation. Therefore, medicine given by aerosol enters the best ventilated parts of the lung and does not penetrate the poorly ventilated parts of the lung where it is needed the most. We have found that some patients benefit from epinephrine, in a 1:1,000 solution, given subcutaneously in doses of 0.3 cc. Isoproterenol, aerosolized as a liquid or powder, is sometimes helpful when spasm contributes to bronchiolar obstruction. The patient may take two or three breaths of this three or four times as needed during the day. This rarely gives relief from dyspnea because of the minor part spasm plays in the ventilatory defect of emphysema, but it has the advantage of being readily available to the patient and affording quick subjective relief.

Types of Treatment

Sedatives.—If the patient can be made to breathe comfortably, he does not need sedatives. Treatment should relieve the cause of dyspnea rather than sedate the patient in an effort to have him sleep in spite of troubled breathing. Heavy sedation is hazardous, because sedatives depress the respiratory center and the patient with emphysema, even though he has dyspnea, is hypoventilating. Avoid the use of morphine and codeine. If sedatives are needed, phenobarbital in a dose of 30 to 60 mg. or chloral hydrate in a dose of 1 to 3 Gm. will give mild sedation without respiratory center depression.

Oxygen Therapy.—Oxygen therapy should be used in the patient with emphysema who is acutely ill with a respiratory infection if hypoxemia is a significant problem. Here it is useful in tiding the patient through a critical period. When the infection is over the patient no longer needs the extra oxygen. It is useful in the late stages of the disease to make the patient more comfortable. We try to avoid long-term oxygen therapy until late in the disease. Some patients become addicted to it and have trouble getting along without it. Dangers accompany the use of oxygen therapy. Since the patient with far-advanced emphysema has pulmonary insufficiency for oxygenation and carbon dioxide elimination, his main stimulus to ventilation is from the chemoreceptors in the carotid and aortic bodies. These receptors are sensitive to a low partial pressure of oxygen in the arterial blood. When oxygen in the arterial blood is increased, the chemoreceptors no longer send messages calling for increased ventilation. Since the respiratory center in the brain is insensitive to carbon dioxide, hypoventilation may follow with further accumulation of carbon dioxide and eventual carbon dioxide narcosis. It is our policy to give patients oxygen therapy intermittently for 20 or 30 minutes each hour.

Breathing Exercises.—A number of physicians who treat patients with pulmonary emphysema have been enthusiastic about the benefits of breathing exercises. The patient needs to have a clear understanding of the pathophysiology of his disease. He may have already learned to breathe out slowly and with pursed lips. If he has been told that this type of breathing actually helps to hold his airways open during expiration, it reinforces what he has found out for himself. The success of breathing exercises depends on the enthusiasm of the physician and the attractiveness of the physiotherapist. In our experience the patients use these exercises faithfully for a while, but as time goes along they tend to abandon them.

Intermittent Positive-Pressure Breathing.—For a while it was hoped that a new gadget, the Bennett valve, was going to be the answer to the problem of emphysema. The initial enthusiasm for this device has now worn off. Although it is helpful in some cases, it is not helpful in the majority. The principle of the machine is as follows: As soon as the patient starts to breathe in, a valve opens and provides air or oxygen at a constant flow. When inspiration stops, the pressure goes on being applied until it reaches a preset point at which the valve turns off and an exhaust opens. Thus, at the end of the patient's normal breath, additional gas is forced into the lung which distends the lung. The patient with emphysema has little trouble getting air in. His main problem is blowing his air out. A disadvantage of the apparatus is that it gives no help in expiration, where the help is desperately needed. A hazard of the apparatus is that the gas goes to the best ventilated parts of the lung. If the alveolar walls in these areas are thin, there is a chance of rupture of the alveoli or even rupture of the lung, especially if the machine has been set to appreciably overdistend the lung. Fowler and coworkers [2] and Leslie and associates [3] have studied intermittent positive-pressure breathing in patients with emphysema. They found that it was an elegant way to administer bronchodilator drugs but that there was little or no benefit from the positive pressure itself.

Steroid Therapy.—Steroids are of little value in the treatment of primary emphysema. Enthusiastic reports regarding steroid therapy in patients with emphysema are the result of their use in patients with bronchial asthma and secondary emphysema. Patients with bronchial asthma respond well to steroid therapy. This reemphasizes an earlier point: it is extremely important to discover the cause of the patient's emphysema. If emphysema is secondary to another type of lung disease, the primary treatment should be aimed at the underlying lung disease.

Pneumoperitoneum.—The administration of air into the peritoneal cavity to raise the diaphragm and improve the expansion of the lung has been advocated for a number of years. The theory is that in emphysema the diaphragm becomes flat at the end of expiration instead of concave or saucer shaped. Air under the diaphragm tends to restore the normal shape to the diaphragm by providing positive pressure from below. The lungs, however, may compensate for this increased pressure from below by increasing the anteroposterior diameter at the end expiratory position so that when the patient is ready for the next breath his vital capacity is unchanged, although a greater proportion of the vital capacity comes from movement of the diaphragm than it did previously. This therapy is still used some, but there is little objective evidence to support it.

Artificial Ventilation with a Respirator.—The respirator does have a definite place in the treatment of patients with respiratory acidosis. In this situation the main problem is hypoventilation. If the patient can receive adequate ventilation to oxygenate the blood and eliminate carbon dioxide from the blood, he will be improved. We find it most useful in patients who have severe emphysema and an acute infection. One disadvantage is that many patients have great difficulty in adjusting their normal ventilation to that of the respirator. Such conflict may make the patient worse instead of better. Under these circumstances, intermittent positive-pressure breathing which is initiated by the patient's inspiratory efforts may be helpful. Another disadvantage is that adequate respirator care requires trained physicians, nurses, and attendants. This arrangement usually can be found only in a large hospital center.

Smoking.—Lowell and co-workers[4] have presented statistical evidence which suggests that smoking is a cause of pulmonary emphysema. We have seen severe emphysema in a few patients who have been nonsmokers. Although this suggestion is held valid by some, it is not established. In our patients with emphysema, we recommend that they stop smoking if possible. We do not demand that they do so. Some patients are happier if they can still smoke a few cigarettes a day, and we have been willing to make this compromise.

Surgery.—Surgical removal of part of the lung in emphysema has been recommended. The theory is that if a portion of the lung is cystic and overdistended it compresses and prevents proper function of adjacent normal lung tissue. This has been demonstrated in patients with localized cysts of the lung. In the generalized form of the disease, however, removal of one section of the lung results in overdistention of another section and is of no benefit to the patient. In our experience this has not been a helpful procedure, and we do not recommend surgical removal of parts of the lung in the patient who has generalized emphysema.

Summary and Conclusions

It is important to differentiate primary emphysema from emphysema secondary to other types of lung disease. When emphysema is secondary to asthma or other lung disease, therapy should be directed to the primary disease. When emphysema exists as a primary disorder, the aims of therapy are to preserve lung tissue, keep the patient active, and make him comfortable.

Preservation of lung tissue is done by treating all respiratory infections vigorously. The patient with emphysema should be urged to continue work whenever possible. He may exert himself to the point of dyspnea. He can be made more comfortable by means of medication; however, care must be exercised in the selection of the proper drugs so that secretions are not dried out and the respiratory center is not depressed. There is no magic device which is the answer to the problem of pulmonary emphysema. The responsibility of the physician is to give the patient a clear understanding of his disorder and to counsel him concerning how his life can be regulated within the limitations imposed by this disease. In emphysema, as in other diseases, the patient needs a physician and not a gadget.

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AGE AND TASTE SENSITIVITY.—A sipping technique was used to test 100 subjects, aged 15 to 89, for taste sensitivity to substances of a sweet, sour, salty, and bitter nature. It was found that the curve of development and decline for sensitivity to each of the 4 taste primaries was essentially the same. All curves showed a noticeable decline after the late fifties. No sex differences were observed nor were there any differences in taste sensitivity between smokers and nonsmokers. . . . The decreasing sensitivity to taste with age is probably due to certain degenerative changes occurring in the taste receptors. . . . Anatomical studies indicate that such changes do occur. Allara reports that the gustatory papillae reach full development at puberty and that regressive changes set in after the age of 45. Furthermore, both Machizuki, studying the foliate papillae, and Arey, Tremain, and Monzingo the circumvallate papillae, report a decrease in number of papillae with age. In addition to a decrease in number of papillae there is also a decrease in number of taste buds. Arey and associates report that in young adults there are approximately 250 taste buds in each circumvallate papilla; over the age of 70 there are less than 100.—R. M. Cooper, I. Bilash, and J. P. Zubek, *Journal of Gerontology*, January, 1959.

RADIOACTIVE ZINC IN THE PROSTATE

SOME FACTORS INFLUENCING CONCENTRATIONS IN DOGS AND MEN

George R. Prout Jr., M.D., Michael Sierp, M.D.
and
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The concentration of zinc in the prostate gland was studied in dogs with prostatic fistulas by injecting the radioactive isotope Zn^{65} intravenously. The ability of the canine prostate to concentrate and secrete zinc was demonstrated. The amount of zinc stored in the gland decreased after orchiectomy and increased greatly after administration of testosterone. It was also found possible to study the concentration of zinc in the human prostate by the preoperative intravenous injecttion of 108 to 150μc of Zn^{65} and the subsequent examination of normal and abnormal prostatic tissue removed in such operations as radical cystectomy. The normal prostate contained more Zn^{65} than did any other normal tissues examined, and neoplastic prostatic tissue generally contained less than normal prostatic tissue or tissue manifesting benign hyperplasia.

The first measurement of zinc in the prostate by Bertrand and Vladesco [1] in 1921 resulted in subsequent experiments designed to clarify the role of this trace metal in the mammalian prostate. Mawson and Fischer [2] have shown that the prostate contains a higher concentration of zinc than do any of the other soft tissues they measured in the human. They demonstrated that concentrations of zinc in normal prostatic tissue and benign hypertrophy are about equal but that prostatic carcinoma and prostatic infection are associated with decreased concentrations of zinc. Hoare, Delory, and Penner [3] found low zinc values in benign hypertrophy and prostatitis and even lower concentrations in carcinoma. Gunn and Gould [4] have demonstrated a difference in the concentration of radioactive zinc between the lateral and dorsal prostate of the rat, also that localization of concentrations of zinc occur in these structures under various endocrine influences.

With the use of dogs prepared with prostatic fistulas, we have previously demonstrated that the intravenously injected radioactive isotope of zinc, Zn^{65}, will appear in a highly predictable manner after stimulation with pilocarpine sulfate for at least 150 days and that concentration of radioactivity was nearly always greater in the first portion of dog prostatic fluid collected.[5] Biopsy of several organs in an intact dog seven days after the injection of 100 μc of Zn^{65} revealed far more radioactivity in the prostate than in any other organ sampled. Estradiol produced a rapid drop in volume and in both concentration and total amount of radioactivity in dog prostatic fluid.[5] Daniel and co-workers [6] demonstrated that intravenously administered Zn^{65} is concentrated in the human prostate and, by radioautographic techniques, they localized the Zn^{65} to the prostatic epithelium.

Methods and Material

Prostatic fistulas were created by the technique of Huggins.[7] After recovery, prostatic stimulation was accomplished by giving 5 mg. of pilocarpine sulfate (1 mg. per milliliter) intravenously at time zero. Dog prostatic fluid (DPF) was collected in two time-determined aliquots, the volume estimated, and the fluid volumetrically transferred to 5-ml. counting vials. DPF 1 was collected from time zero to 15 minutes and DPF 2 from 15 to 30 minutes after administration of pilocarpine.

The radioactive isotope of zinc, Zn^{65}, was obtained as zinc chloride with a carrier content of less than 300 mcg. per millicurie. The isotope was administered intravenously in every instance. Radioactivity was determined in a well-type scintillation counter, usually counting 1 or 2 ml. of prostatic fluid. The radioactivity recovered in 1 ml. of prostatic fluid is expressed as a percentage of the total radioactivity administered. This value is expressed as 10^{-3} in the data and is henceforth referred to as radioactivity in dog prostatic fluid.

Tissues obtained by biopsy were placed in preweighed vials and were weighed again immediately. Each vial was then frozen until radioactivity was determined. The percentage of the injected dose in each sample was expressed as radioactivity per gram of wet tissue (10^{-3}). Acetazolamide (Diamox) was injected intravenously immediately before pilocarpine was given or as indicated. The chemical analysis of sodium, potassium, chloride, and the carbon dioxide combining power were carried out according to suitable laboratory methods as re-

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ported elsewhere.[8] The hydrogen ion concentration of the prostatic fluid was estimated at 1 minute and 17 minutes after the injection of pilocarpine, with the use of pHydrion indicator paper. Crystalline preparations of testosterone and estradiol were given intramuscularly as indicated in the animal experiments. Ethinyl estradiol or chlorotrianisene (Tace) was given to men as indicated.

TABLE 1.—*Radioactivity in Canine Prostate*

	Intact			Testosterone 10 Mg./Day	Estradiol 12.5 Mcg./Day	Orchiectomy Performed Day Zero
Dog	X227	X22	X4	X371	X344	X262
Zn^{65} µc	255	250	100	146	146	195
Days after injection						
5	39	22	...	249	169	16
7	...	...	300	...	...	...
14	133	152	...	731	105	4

Experiments on Dogs

EXPERIMENT 1.—Six dogs were involved in this experiment. Dogs X22 and X227 were given, respectively, 250 and 255 µc of Zn^{65}, and biopsies were performed on the prostates at 5 and 14 days thereafter. There were higher concentrations of radioactivity in the second biopsy specimens. Dog X4 was given 100 µc of Zn^{65}, and a biopsy was performed on the prostate on the seventh day. The concentration of radioactivity was greater than in any of the specimens taken from the other dogs, except the one influenced by testosterone.

Dog X371 was given 146 µc of Zn^{65} on day zero and also started on therapy with testosterone, 10 mg. intramuscularly daily. Biopsy specimen on the fifth day showed far greater concentration of radioactivity than did the controls (dogs X22 and X227). At 14 days, exogenous testosterone administration was associated with a continued pronounced rise in concentration of radioactivity to about five times the values in the control studies.

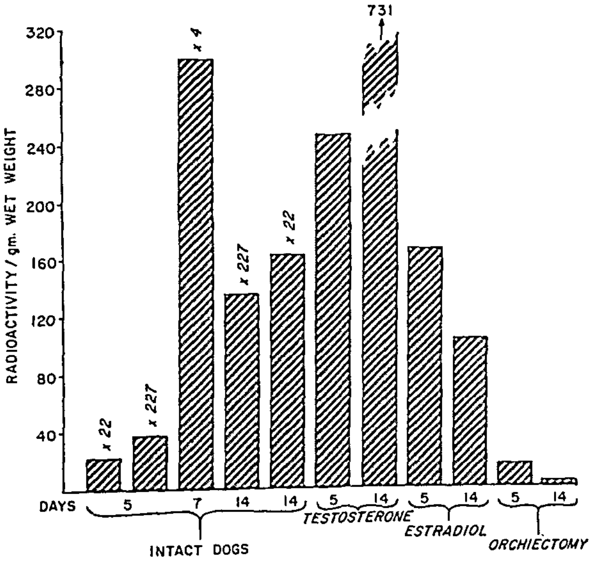

Fig. 1.—Radioactivity in canine prostate.

Dog X344 was given 146 µc of Zn^{65} on day zero and was also started on therapy with estradiol, 12.5 mcg. intramuscularly daily. Dog X262 was given 195 µc of Zn^{65} on day zero and was castrated on the same day. These dogs were also subjected to prostatic biopsy on the 5th and 14th days. Results are shown in table 1 and figure 1.

EXPERIMENT 2.—After a prostatic fistula had been constructed and a control period of 21 days completed, dog X55 received testosterone, 10 mg. daily intramuscularly. Fourteen days later bilateral orchiectomy was carried out and five days after that the dog was injected with 129 µc of Zn^{65}. Prostatic fluid was obtained at varying intervals thereafter. The results are shown in table 2 and figure 2.

Prior to the institution of exogenous testosterone, the volume of DPF produced and the concentration of radioactivity were both low in dog X55. When testosterone was given daily and the dog subsequently castrated, the volumes of DPF 1 and 2 were maintained at average levels of nearly 20 ml. and 8 ml. respectively. Radioactivity in DPF 1 and 2 reached peaks of 56 and 32 on the 7th day, and 14 and 6 on the 38th day after injection of 129 µc of Zn^{65}.

TABLE 2.—*Radioactivity and Volume of Dog Prostatic Fluid in Dog X55 Given 106 µc of Zn^{65} on Day Zero*

	Radioactivity			Volume, Ml.	
Days	DPF1†	DPF2†		DPF1†	DPF2†
1	15	...‡		3.5	...‡
4	13.5	4.0		4.0	1.5
7	5.0	5.0		3.0	3.0
10	13.0	8.0		8.0	3.5
14	7.5	1.5		8.0	4.0
18	5.0	2.0		4.0	...‡
21	2.0	1.5	←Testosterone 10 mg. daily commenced→	8.0	4.0
24	2.5	2.0		13.0	5.0
28	2.1	1.0		16 0	6.0
31	1.5	1.0		18.0	7.0
35	1.5	1.0	←Bilateral orchiectomy→	18.0	5.0
39	2.0	1.0		13.0	5.0
			← Zn^{65} 129 µc day 40 →		
42	2.0	1.0		20.0	5.0
49	56.0	32.0		20.0	5.0
52	41.5	20.5		25.0	9.0
56	38.0	21.0		20.0	5.0
59	29.0	11.0		24.0	6.0
64	21.0	10.0		21.0	11.0
69	19.0	9.0		19.0	9.0
71	10.0	9.0		15.0	5.0
75	13.0	6.5		17.5	9.0
78	14.0	6.0		20.0	5.0

†DPF1 = fluid collected 0 to 15 minutes; and DPF2 = from 15 to 30 minutes after injection of pilocarpine.
‡ DPF1 and DPF2 combined.

EXPERIMENT 3.—Dog X75, after complete recovery from the creation of a prostatic fistula, was given 66 µc of Zn^{65}. DPF was collected at varying intervals thereafter. Details of this experiment are published elsewhere.[5] The results are shown in table 3 and figure 3.

EXPERIMENT 4.—Control studies on the ionic constituents of DPF 1 and 2 were obtained. Acetazolamide was given intravenously at time zero in amounts varying between 95 and 128 mg. per kilogram to several different dogs in which prostatic fistulas had been created. The results of this experiment are shown in table 4.

Control studies on the ionic constituents of prostatic fluid need little comment. The potassium level was always less in DPF 2 than in DPF 1, the average values being 6.6 mEq. and 3.9 mEq. per liter. Sodium was nearly always less in DPF 1 than in DPF 2, the average values being 149 mEq. and 152 mEq. per liter. The same was true of the chloride, the average values being 161 mEq. per liter for DPF 1 and 162 mEq. per liter for DPF 2. Bicarbonate ion was so low as to constitute a qualitative rather than a quantitative assay. When acetazolamide was given intravenously, no remarkable departure from the control studies could be detected.

Experiment 5.—After complete recovery from the creation of prostatic fistulas and after orchiectomy and the institution of testosterone therapy, 10 mg. intramuscularly daily, dogs X656 (weight 26 kg.) and X266 (weight 16 kg.) were given 272 μc of Zn^{65} each on day zero. Acetazolamide in 100 mg. per kilogram dose was given intravenously thrice to the former and four times to the latter. Volume and radioactivity in DPF 1 and 2 were recorded. The results are shown in table 5 and figure 4.

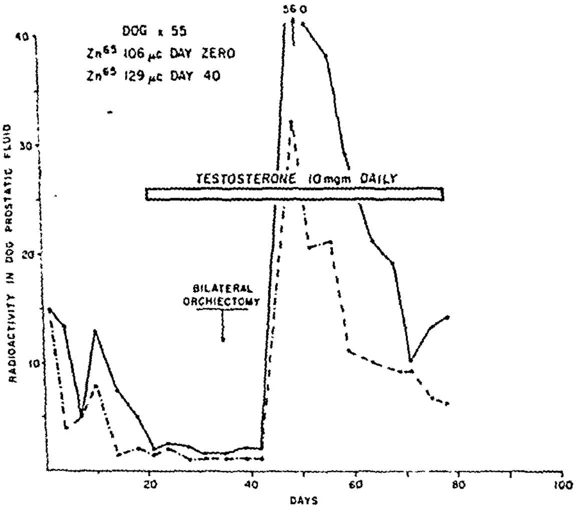

Fig. 2.—Radioactivity in prostatic fluid of dog X55. Solid line *indicates fluid collected from 0 to 15 minutes; dotted* line, from 15 to 30 minutes after injection of pilocarpine.

When acetazolamide was given to dogs who had received Zn^{65}, a peak of 71.4 in DPF 1 was seen in dog X266, but subsequent concentrations of this magnitude were not observed in this animal nor in dog X656, whose highest value of radioactivity was 21.7. No remarkable alteration in the concentration of radioactivity occurred in DPF 2 in either animal nor in the volume produced.

Estimation of the hydrogen ion concentration in experiments 4 and 5 was done more than 50 times. The pH controls revealed a usual decrease in pH from 5.5 to 5 between DPF 1 and 2. Occasionally the pH was as high as 6 or as low as 5 in DPF 2, and occasionally the decrease in pH in DPF 2 failed to occur. Administration of acetazolamide failed to alter these patterns in any way.

Report of Cases

Men with various urologic disorders were given between 108 and 150 μc of Zn^{65} intravenously, and tissue was subsequently obtained at operation by sharp dissection and never washed or immersed in fluid. The posterior lamella of the prostate was separately assayed when it could be distinctly identified. The prostatic tissue designated as "normal" was obtained *immediately after radical cystectomy* in each instance. Cowper's gland was removed in each instance during perineal dissection. Each anatomic and pathological diagnosis was substantiated histologically. Minor inflammatory responses were ignored in the pathological diagnosis. Only the major histological feature of each gland was recorded. Radioactivity in the blood is not

Table 3.—*Radioactivity and Volume of Dog Prostatic Fluid in Dog X75 Given 66 μc of Zn^{65} on Day Zero*

Days After Injection	Radioactivity		Volume, Ml.	
	DPF1†	DPF2†	DPF1†	DPF2†
1	29.9	17.1	6.0	5.0
3	25.9	17.6	8.0	4.5
6	34.0	19.9	10.0	5.0
8	20.0	15.4	8.0	4.0
11	24.3	11.5	9.0	5.0

† DPF1 = fluid collected 0 to 15 minutes; DPF2 = from 15 to 30 minutes after injection of pilocarpine

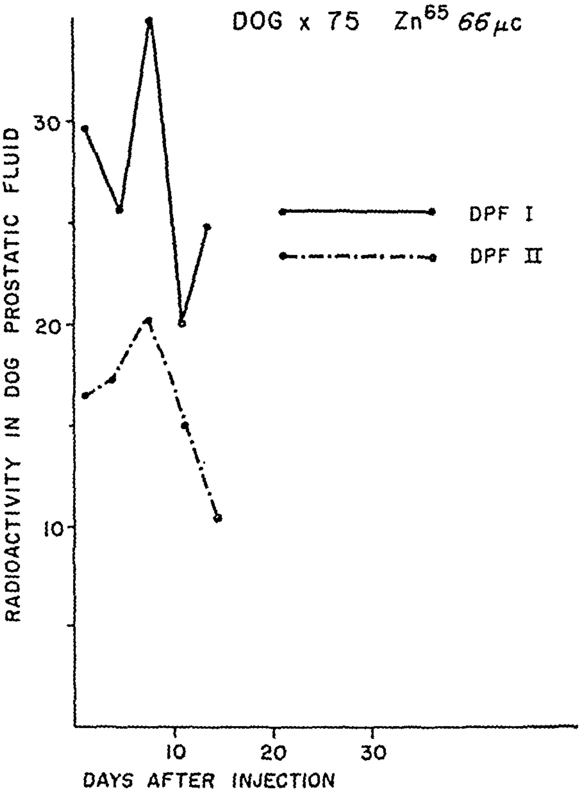

Fig. 3.—Radioactivity in prostatic fluid of dog X75.

shown because many of the patients received transfusions in varying amounts during the surgical procedures.

Case 6.—A 60-year-old man had undergone an abdominal-perineal resection for adenocarcinoma of the rectum 20 years prior to admission for progressing signs of bladder neck obstruction. A transurethral resection was carried out and adenocarcinoma was diagnosed histologically. Two days after the administration of Zn^{65}, a radical cystectomy was carried out. The prostate was small and seemed fibrotic. A biopsy was taken of the more centrally placed portion of the prostate for the determination of radioactivity. Aside from scant inflammatory response, adenocarcinoma was again noted.

Case 7.—A healthy, sexually active, asymptomatic, 62-year-old man was told during a routine physical examination that he had a nodule in his prostate. The nodular area was confined to the capsule of the right lobe and measured about 10 mm. in greatest diameter. Two and a half days after the injection of Zn^{65}, perineal exploration and biopsy of this nodule and the opposite prostatic lobe were performed and specimens submitted for histological examination and radioactivity assay. Carcinoma was present in the nodule only.

Case 9.—An 81-year-old male had undergone three transurethral resections for an infiltrating carcinoma of the bladder and had also had partial transurethral resection of the prostate prior to radical cystectomy. He was in good health aside from cardiovascular disease. The prostate was enlarged with a firm nodule on its posterior surface that was suggestive of primary carcinoma. Zn^{65} was given a day and a half before operation. A portion of the posterior lamella of the prostate stripped readily from the radical cystectomy specimen, was separately excised, and the radioactivity determined. A deeper section of the prostate was also excised and the radioactivity determined. Histological sections of the prostate revealed adenocarcinoma in addition to some inflammatory response.

Table 4.—*Control Determinations and Effect of Intravenously Administered Acetazolamide on Ionic Constituents of Dog Prostatic Fluid*

Control†	Sodium, mEq./Liter	Potassium, mEq./Liter	Chlorine, mEq./Liter	Bicarbonate Radical, mM./Liter*
DPF1‡	149	6.6	161	1.8
DPF2	152	3.9	162	1.3
After Acetazolamide				
DPF1	147, 145, 147, 149	5.8, 6.2, 6.5, 5.8	160, 161, 163, 170	1.8, 2.4, 5.4, 1.3
DPF2	153, 153, 146	4.3, 4.3, 2.6, 3.8	165, 163, 163, 163	2.0, 2.0, 1.8, 1.7

* Fluid collected under oil.

† These figures represent an average of not less than 10 determinations in each category.

‡ DPF1 = fluid collected from 0 to 15 minutes; DPF2 = from 15 to 30 minutes after injection of pilocarpine.

Case 12.—A 70-year-old man had been treated by transurethral resection for sarcoma of the prostate. The sarcoma could be felt at the base of the right lobe extending into the region of the right seminal vesicle. Four days after the injection of Zn^{65}, a radical cystectomy was performed and sections from the tumor, the uninvolved posterior lamella, and the more centrally placed prostatic tissue were examined for radioactivity.

Case 17.—A 70-year-old man had minimal urinary symptoms and was in good general condition. A firm, 12-mm., nodular mass was palpable at the base of the prostate. After exposure perineally, this mass was thought to be an area of adenomatous hyperplasia with infection present. This impression was corroborated histologically. The radioactivity present in the capsule and hyperplastic prostate was determined.

Concentrations of Radioactivity in Human Tissues

In each of the three patients whose prostates were considered normal, the concentration of radioactivity was higher in the prostate than in any of the other tissues on which biopsy was performed. The values for prostatic radioactivity in these three patients ranged from 14.0 to 5.3. In the one patient in whom the radioactivity of Cowper's gland was determined, the concentration was 3.8 (table 6).

Two of the patients suffering from carcinoma of the prostate were in relapse. Orchiectomy had been done two years previously in case 15 and six months earlier in case 13. These two patients had concentrations of 4.4 and 5.6, respectively, in their prostatic tissue. Lymph nodes removed from one during celiotomy were found to have tumor tissue present, with activities of 5.7, 6.3, and 7.8 (table 7).

One man (case 14) was given chlorotrianisene for six months without benefit of histological diagnosis of cancer. The clinical diagnosis of cancer was confirmed by biopsy of his prostate six weeks after the last dose of chlorotrianisene and three days after Zn^{65} had been given. In this patient and in eight other untreated patients with carcinoma of the prostate, the radioactivity in the prostate ranged from 12.7 to 1.8, the average being 5.5. Radioactivity in the isolated case of sarcoma of the prostate was 5.6 (table 7, case 12).

In one patient (case 7) the sharply demarcated malignant area in the prostate had a concentration of 5.1, while the adjacent tissue had a concentration of 9.6. In another man (case 9) the posterior lamella, presumed free of disease, was 6.8. This sample of tissue as well as corresponding samples obtained from the prostates of two other patients (cases 12 and 13) were not examined histologically, but no doubt exists as to the over-all diagnosis in the individual prostates (table 7).

In the other genital appendages and testes on which biopsy was performed, concentration of radioactivity was always less than in the prostate, except in one man (case 5) whose epididymis had a radioactivity of 7.1 as opposed to 6.8 for prostatic radioactivity and in another man (case 10) whose testis had only slightly greater activity than the prostate. Epididymal concentrations of radioactivity ranged from 0.9 to 7.1, and testicular concentrations from 1.6 to 3.3. Radioactivity in the vas varied from levels too low to be significant to 4.2 (table 7).

Of the nine patients with benign prostatic hyperplasia, the adenomas contained concentrations of radioactivity varying from 22.1 to 3.2, while the capsular concentration varied from 8.6 to 2.1 (table 8). Three men (cases 21, 22, and 23) received estrogen therapy in association with the administration of isotope and before prostatectomy. In these three the adenomas had radioactivity varying between 7.7 and 7.0. In two the capsular concentrations of radioactivity were 8.4 and 3.6, and in one of these was seen the greatest concentration of radioactivity in the vas (6.6). Another patient received exogenous testosterone therapy and had a concentration of radioactivity of 10.6 in the adenoma and 2.1 in the capsule. The concentrations of radioactivity in the seminal vesicle of intact men not receiving hormone treatment varied from 0.7 to 4.6. In the one patient in this group in whom the radioactivity of Cowper's gland was determined, the concentration was 2.2 (table 8).

Dog Prostatic Fluid

Since it has been demonstrated that after the intravenous administration of radioactive zinc, Zn^{65}, the concentration of that isotope in dog prostatic fluid is related to time as well as to health and general condition,[9] it seems reasonable to expect a reflection of this phenomenon in the concentration of radioactive zinc in the prostate. As demonstrated, such is the case (experiment 1, table 1, fig. 1). It is probable that we have missed the actual peaks of concentrations, especially in the prostatic tissue, but from data concerning radioactivity in DPF 1 and DPF 2[5] as well as from information regarding prostatic biopsies,[9] it seems reasonable to conclude that although each animal concentrates Zn^{65} in an individual manner, most dogs probably reach a peak of concentration within two weeks. It seems unlikely that the peak of concentration of radioactivity in prostatic fluid occurs much before five days.

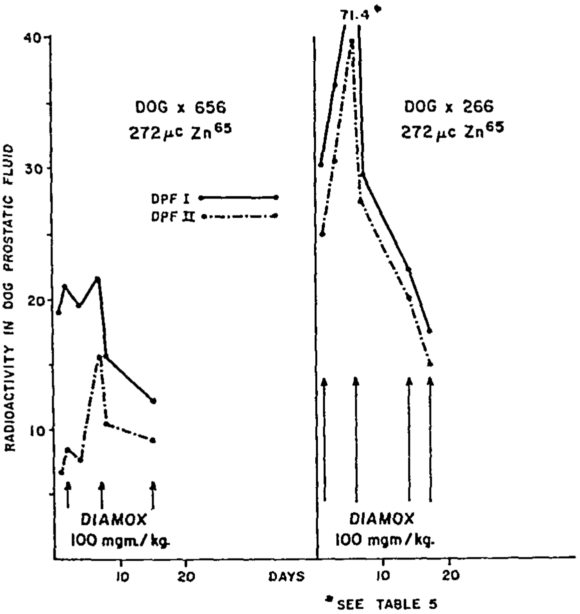

Fig. 4.—*Effect of acetazolamide (Diamox) on Zn^{65} in dog prostatic fluid.*

TABLE 5.—*Effect of Acetazolamide on Volume and Concentration of Zn^{65} in Dog Prostatic Fluid*

Days After Injection of Zn^{65}	Radioactivity DPF1†	Radioactivity DPF2†	Volume, Ml. DPF1†	Volume, Ml. DPF2†	Acetazolamide, Gm.
Dog x 656 Zn^{65} 272 μc					
1	19.2	6.8	20.0	9.0	
2	21.0	8.5	19.0	8.0	2.6‡
4	19.6	7.8	27.0	8.0	
7	21.7	15.7	18.0	5.5	2.5
8	15.8	10.4	21.0	6.5	
15	12.3	9.2	33.0	6.5	2.5
Dog x 266 Zn^{65} 272 μc					
1	30.4	25.0	36.0	8.5	1.6
3	36.5	30.7	32.0	2.5	
6	71.4§	40.0	8.0	8.0	1.6
7	29.4	27.6	30.0	9.5	
14	22.3	20.3	32.0	11.0	1.5
17	17.5	15.0	37.0	9.0	1.5

† DPF1 = fluid collected 0 to 15 minutes; DPF2 = from 15 to 30 minutes after injection of pilocarpine.

‡ Given at 15 minutes; rest given at 0 minutes.

§ First portion lost.

Huggins and associates[10] observed that caged dogs responded to their environment by becoming azoospermic. Weight loss, shedding, and loss of appetite are other manifestations of an adverse response to caging. It is impossible to ascertain the amount of prostatic fluid such dogs might produce under natural conditions. Most impressive is the response in terms of exaggerated production of DPF to exogenous testosterone when compared to the control period in the same dog or to other dogs dependent on endogenous androgen alone. There is also a remarkable increase in the concentration and total amount of radioactive zinc produced during the period of testosterone administration as compared with the control period in the same animal (experiment 2, table 2, fig. 2). It is conceivable that the lesser volumes and radioactivity we usually collect are the result of decreased gonadotropin production, while the response to exogenous testosterone represents more nearly the normal physiological state. Leaving these considerations aside, it is clear that the presence of radioactive zinc in the prostate and dog prostatic fluid is an androgen-dependent phenomenon, be it endogenous or exogenous in origin.

It is of interest that the total amount of Zn^{65} produced in one hour reaches relatively high levels, particularly during the first two weeks after the injection of the isotope. Dog X75 has been demonstrated to produce volumes and concentrations of radioactivity in DPF 3 (prostatic fluid secreted between 30 and 60 minutes) that are usually equal or slightly lower than those found in DPF 2.[5] Since Huggins and associates [10] have shown that 95% of the volume of prostatic fluid is produced in one hour after pilocarpine injection, the amount of radioactivity produced by X75 on any of the days shown can be calculated from table 3, assuming that total radioactivity found in DPF 3 is 90% of that found in DPF 2. Though some objection may be raised, this maneuver seems reasonable in view of this animal's previous performance.[5] Hence, on the sixth day after the injection of the isotope, about 0.54% of that dose was secreted. On the 8th and 12th days 0.28 and 0.33%, respectively, of the injected isotope was produced (experiment 3, table 3, fig. 3). Unless some hormonal influence, illness, or other catastrophe should occur, the production of DPF and radioactive zinc in similar but ever decreasing amounts will continue. This dog weighed about 18 kg., and his prostate can scarcely have exceeded 10 Gm. in weight.[11] Bearing in mind the observations that the prostates of the intact control animals have maximal concentrations of radioactivity per gram of 0.039% on the 5th day and 0.152% on the 14th day (table 1, fig. 1), it seems that the prostate must be continuously replenishing itself with the isotope rather than storing a maximal concentration during the short initial period of relatively high blood and plasma concentrations. This is buttressed by the observation that X75 and all the other dogs we have studied continued to produce relatively large amounts of isotope in addition to the fact that the control animals were never subjected to the depleting effects of pilocarpine.

TABLE 6.—*Radioactivity in "Normal" Prostate in Carcinoma of the Bladder**

Case	Age	Sexual Intercourse	Day After Zn^{65} Injection	Prostate	Cowper's Gland	Seminal Vesicle	Vas	Epididymis	Testis	Striated Muscle
1	63	?	5	9.6	3.8	3.3	3.9	5.9	2.8	...
2	69	?	2	14.0	...	1.0	...	...	1.6	3.8
3	54	Once a wk.	4	5.3	...	4.0	...	...	...	1.0

*All patients were in good general condition.

We are unable to explain the alterations in the concentrations of isotope in dog prostatic fluid [5] (fig. 2, 3, and 4) and in the prostate over the first two-week period of observation. It is conceivable that Zn^{65} is being incorporated into a protein complex and that this is a time-consuming process evidenced by the lag in maximal concentration in both gland and fluid. If such were the case, one would not expect the prostate to be able to produce the relatively large amounts of isotope that it does on repeated stimulation in view of the known prostatic concentration.

Orchiectomy produces a prompt, impressive decrease in the concentration of Zn^{65} in the dog prostate. Fourteen days after orchiectomy, the concentration of radioactive zinc in the canine prostate is only 3% of the lower control value (dog X22, table 1). When estradiol was given, the volume and the concentration and total amount of Zn^{65} produced were decreased.[5] The decrease in the volume of prostatic fluid produced is more readily assessed than the alteration in Zn^{65} secretion but prostatic biopsies reveal a distinct decrease in Zn^{65} concentration. The 14-day value for radioactive zinc concentration during the administration of estradiol is 78% of the lower control value and 69% of the higher (table 1). These values are appreciably higher than those obtained after orchiectomy but it is conceivable that, had we waited for a longer period of time, the radioactivity would have dropped to lower levels. It is clear that orchiectomy acts more promptly and possibly more effectively in decreasing the concentration of Zn^{65} in the prostate than does estradiol.

Since zinc is the prosthetic metal associated with carbonic anhydrase, it seemed reasonable to attempt evaluation of the role of carbonic anhydrase in producing dog prostatic fluid. Huggins [7] has described the ionic constituents of dog prostatic fluid, but to record any acute alterations controls must first be established. Even though Mawson and Fischer [12] have demonstrated that in the prostates of the rat and rabbit there is far more zinc than can be accounted for by the presence of carbonic anhydrase, we felt it worthwhile to measure the concentration of Zn^{65} in the prostatic fluid of dogs after the intravenous injection of relatively large doses of acetazolamide, a substance demonstrated to effectively inhibit carbonic anhydrase activity.[13] We also measured volume and ionic concentrations and crudely estimated the hydrogen ion concentration. Any alteration that occurred in these features seemed to fall within the range of our established norms. The bicarbonate ion may be significantly elevated, but these levels leave doubt as to technical accuracy. It seems reasonable to conclude that acetazolamide does not effectively alter the volume, pH, ionic constituents, or Zn^{65} concentration in either DPF 1 or DPF 2. We do not necessarily conclude that carbonic anhydrase plays no role in the production or constitution of dog prostatic fluid (experiments 4 and 5, tables 4 and 5, fig. 4).

Prostatic Concentrations in Men

Acetazolamide was given in doses as high as 1 Gm. daily to six men with prostatic adenocarcinoma. No objective or subjective alteration in the patients' courses could be ascertained, even in terms of hours. When Zn^{65} was injected intravenously into men with no prostatic disorder, the prostate contained significantly more isotope than the other tissues on which biopsy was performed. Intact men with carcinoma of the prostate also had a higher concentration of Zn^{65} in their respective neoplastic glands than in nearly all of the other tissues. In general, the trend of the values is lower in the neoplastic gland than in the "normal" prostates or in the adenomas of benign hyperplasia. There are five determinations below 5.0 in the carcinoma group and only one below 5.0 in the "normal" and adenomatous groups. The sum of the patients without neoplasia makes a numerical group suitable for comparison with those intact patients with carcinoma (tables 6, 7, and 8). We were able to demonstrate that one clearly neoplastic area contained less Zn^{65} than adjacent histologically normal prostatic tissue (table 7). It would be erroneous to conclude that neoplastic tissue had less Zn^{65} in it except at the time biopsy was performed were it not for data published by Mawson and Fischer[14] on untreated patients with carcinoma of the prostate and Hoare and co-workers[3] indicating that total zinc concentrations in the neoplastic gland are unquestionably lower than in the normal gland. Hence, one might reasonably suppose that the malignant gland would have less Zn^{65} at any given time after injection of the isotope than the "normal" gland.

TABLE 7.—*Radioactivity in Neoplastic Prostate*

Case	Age	General Condition	Sexual Intercourse	Days After Zn^{65} Injection	Neoplasm	Adjacent Normal Prostate	Lymph Node Metastases	Seminal Vesicle	Vas	Epididymis	Testis	Striated Muscle
4............	68	Fair	?	4	2.1	...	...	...	x, x	0.9 0.9	1.7 1.6	...
5............	53	Excellent	Twice a wk.	2	6.8	...	...	...	...	7.1	..	...
6............	60	Good	?	2	1.8	...	...	0.7	...	...	...	...
7............	62	Excellent	Twice a mo.	2.5	5.1	9.6	...	2.8	4.2	4.4	2.4	...
8............	67	Good	?	3	12.3	...	...	...	...	...	...	0.6
9............	81†	Good	Once a mo.	1.5	4.8	6.8 Posterior lamella	...	...	...	...	...	0.7
10............	69	Good	0	7	2.9	...	...	...	...	2.1	3.3	1.2
11............	65	Fair	0	2	2.5	...	...	...	...	1.6 1.9	2.1 1.9	.
12............	70‡	Good	?	4	5.6	4.0, 6.9 Posterior lamella	...	...	...	...	...	1.0
13............	67§	Fair	0	2	5.6	4.5 Posterior lamella	6.3, 5.7, 7.8	...	...	...	...	1.4
14............	74‖	Good	?	3	12.7	...	...	...	...	...	...	1.1
15............	59¶	Poor	0	10	4.4	...	...	...	...	...	...	2.1

† Carcinoma of bladder and prostate.
‡ Sarcoma of prostate.
§ Anaplastic carcinoma of prostate. Orchiectomy performed six months before administration of isotope.
‖ Chlorotrianisene therapy discontinued six weeks before biopsy.
¶ Orchiectomy two years, estrogen stopped six months prior to isotope administration.

Daniel and co-workers[6] have reported on Zn^{65} prostatic concentration in 12 patients with various diseases. They chose to report organ/blood ratios rather than percentage of injected dose of isotope. Since many of our patients received considerable volumes of blood during exenteration, and for other reasons as well, it was determined inadvisable to show organ/blood Zn^{65} ratios. Expression of the data presented by Daniel and co-workers as percentage of injected isotope reveals no remarkable departure in values from those we have presented here except for one patient with adenocarcinoma of the prostate. This man's concentration of prostatic radioactivity was 28, a figure over twice our greatest concentration in patients with this disease. Until more information is accumulated, this concentration must be viewed as a departure from the usual trend.

Orchiectomy was not associated with a dramatic decrease in Zn^{65} concentration in the neoplastic gland. For points of reference one may refer to the unaltered concentration of Zn^{65} in striated muscle (table 7). We have to date not done the obvious experiment of taking a biopsy specimen of the prostate before and after orchiectomy. The lymph nodes in which metastatic disease was present all had radioactivity comparable to that of the primary tumor. Retrospection makes obvious the need for radioactivity determinations in uninvolved nodes.

From the data regarding radioactivity in benign hyperplasia, it is suggested that the prostate capsule contains less radioactivity than the adenoma. We took biopsy specimens from these patients at intervals of one and one-half to seven days after Zn^{65} administration and can only state that during these periods more Zn^{65} was concentrated in the adenoma than in the capsule of the individual gland (table 8). When estrogen was given with, before, or after Zn^{65}, no alteration in concentration of the isotope could be detected from the control levels. The only published data on the effect of stilbestrol on zinc concentration in the human prostate are those of Hoare and associates.[3] They were able to demonstrate a slight decrease in total zinc concentration, roughly approximating our determinations utilizing Zn^{65}. Exogenous testosterone was not associated with any clear-cut alteration in isotope concentration in the single experiment reported (table 8).

Comment

It seems inappropriate to attempt direct application of canine data to human data concerning Zn^{65}. Species difference, difference in relative mammalian age, and prostatic size are obvious objections. This may be particularly true when widespread metastases from carcinoma of the prostate are present. It is conceivable that in our present state of ignorance regarding trace element physiology, we have failed to account for the dilution of the isotope that takes place as a result of the disparity in body mass between mammals, and that, in competing for zinc with other organs, the human prostate does not concentrate the isotope as the dog's does. Nevertheless, it would seem that our canine orchiectomy and testosterone responses are so unequivocal that some alteration in Zn^{65} concentration would be demonstrable in man.

Table 8.—*Radioactivity in Benign Hyperplasia of the Prostate**

Case	Age	Sexual Intercourse	Days After Zn^{65} Injection	Adenoma	Posterior Lamella	Cowper's Gland	Seminal Vesicle	Vas	Epididymis	Testis	Striated Muscle
16	68†	Twice a mo.	3	5.6	2.2	...	3.5	...	...	...	0.9
17	70‡	0	7	22.1	8.6	...	3.7	...	...	...	2.0
18	71†	Yes Amt. ?	1.5	8.2	7.4	...	4.4	3.3	...	...	0.5
19	65†	?	2	6.2	2.4	...	4.6	4.0	3.7	2.3	...
20	73	?	6	3.2	3.4	2.2	...	...	...	...	2.5
21	73§	?	9	7.4	...	...	...	...	...	...	1.4
22	66†‖	Yes Amt. ?	5	7.0	8.4	...	4.0	6.6	...	...	0.9
23	67¶	?	15	7.7	3.6	...	...	...	...	...	...
24	62†#	Yes Amt. ?	4	10.6	2.1	...	0.6	...	...	...	...

*All patients were in good general condition.

† Carcinoma of bladder, also.

‡ Prostatitis also.

§ Ethinyl estradiol therapy, 0.5 mg. daily, for nine days before biopsy.

‖ Ethinyl estradiol therapy, 0.5 mg. daily, for two weeks before biopsy.

¶ Ethinyl estradiol therapy, 1 mg. daily, for 10 days before biopsy.

Testosterone therapy, 25 mg. daily intramuscularly, for one week before biopsy.

The concentrations of Zn^{65} in the human epididymis, vas, and seminal vesicle are relatively low. The feature these values all seem to have in common is that they are not subject to the wide variations that the prostatic values undergo.

We recognize that the data presented here prevent dogmatic conclusions by virtue of statistical inadequacy alone, but the information thus far obtained regarding radioactive zinc in mammalian genitalia would indicate that the propensity displayed by the prostate for Zn^{65} is an androgen-controlled phenomenon that is adversely affected by orchiectomy and the administration of female hormones in the dog. Irregular, unforeseeable concentrations of the isotope have been found in the human prostate, and it would seem that neoplasms and the prostatic capsules of benign glands have lesser concentrations of Zn^{65} than the normal and the adenomatous glands.

Still unanswered is the major question regarding genital zinc. What is its function? As pointed out elsewhere, sperm are richer in zinc than any human tissue studied, yet the testis is relatively poor in this element.[5] From this observation alone, it would seem that zinc is related to spermatic physiology. It is conceivable that the prostate acts as nothing more than a purveyor and receptacle for zinc until ejaculation occurs and at this time zinc is incorporated in the sperm in a perhaps essential capacity. Certainly, under the conditions of the experiments, the unfailing appearance of Zn^{65} in prostatic fluid and the prostate suggests that prostatic fluid without zinc would no longer be prostatic fluid.

Experiments 1 and 2 are results of work by Dr. Michael Sierp and associates[9a] and will be the subject of more detailed reports.

Data on dog X4 (table 1, fig. 1) and data in table 3 and figure 3 are reproduced with permission from Prout and associates.[5]

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INAPPARENT PYELONEPHRITIS—THE MISSING LINK?

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A significant degree of bacteriuria has been found in some cases to exist in the absence of leukocytes in the urine and also in the absence of such urologic symptoms as dysuria, frequency, and nocturia. Autopsies disclose the presence of pyelonephritis in cases where it had not been recognized ante mortem. For these reasons it is suggested that there must exist an asymptomatic stage in the history of pyelonephritis, intervening between the acute stage and the chronic end-stage. Recognition of the asymptomatic stage depends on the development of reliable and safe techniques for detecting bacteriuria. It is essential if the termination in hypertension and uremia is to be prevented.

Inapparent pyelonephritis occupies a pivotal position in the course of pyelonephritis. Both acute pyelonephritis and chronic end-stage pyelonephritis manifested by uremia and hypertension are generally recognized. The link between these apparent phases is less well appreciated. Pyelonephritis has been found in 6 to 20% of autopsies; yet the clinical diagnosis of pyelonephritis was made in only about one-fifth of these cases.[1] This discrepancy suggests a high incidence of inapparent pyelonephritis in the general population. It is the purpose of this discussion to reemphasize the inapparent phase in the natural course of pyelonephritis and to discuss the clinical recognition of inapparent active pyelonephritis. Recognition of this phase is dependent upon safe methods for detecting bacteriuria. The value of quantitative bacterial counts as an aid in the differentiation of contaminating from significant bacteria in urine cultures and the feasibility of employing "voided" urine specimens obtained from both males and females as screening cultures to facilitate the detection of inapparent pyelonephritis will be presented.

Spectrum of Pyelonephritis

The natural course of pyelonephritis is clinically apparent as a series of separate and unrelated events. The patient is seen by different specialists during each episode of infection, which tends to fragment genuine understanding of the course of renal infection. The discrepancy between the frequency of pathological evidence of active pyelonephritis and clinical evidence of acute pyelonephritis suggests that these separate episodes of acute infection may be linked via an active inapparent phase. Pyelonephritis may then be considered as a disease continuum, illustrated hypothetically in the figure.[2] There is additional clinical evidence which suggests the presence of continued active inapparent renal infection. For example, the so-called pyelitis of infancy usually has been considered as a self-limited illness. Long-term reevaluation has failed to justify this optimism (table 1).[3] A striking feature was the frequency of abnormalities, which included at least one of the following conditions: abnormality on intravenous urography, persistent pyuria, or positive urine cultures. The majority of these patients with residual abnormality were completely asymptomatic at the time of follow-up study.

An association between chronic pyelonephritis and arterial hypertension, necrotizing arteriolitis, and uremia was clearly demonstrated by Weiss and Parker.[4] While a direct causal relationship between pyelonephritis and arterial hypertension has not been unequivocally demonstrated, the association is definitely suggestive. The importance of inapparent pyelonephritis as a link between acute renal infection and end-stage pyelonephritis was suggested from the first by Weiss and Parker when they asked the following question: "Are cases of 'silent bacteriurias' benign, or can they cause subsequent hypertension or renal failure? Should they be treated as intensely as those associated with the clinical picture of pyelonephritis?"[5] This question as to the role of inapparent progressive pyelonephritis or "asymptomatic bacteriuria" in the natural history of pyelonephritis has not been clearly defined as yet.

Methods of Recognition

If one accepts the existence of an inapparent active phase as a possible link between episodes of clinically obvious acute pyelonephritis or between acute pyelonephritis and end-stage pyelonephritis, how can this inapparent active phase be detected? Is "silent" or asymptomatic bacteriuria a manifestation of active inapparent pyelonephritis? Evaluation of asymptomatic bacteriuria is dependent on methods for the differentiation of infection from contamination during collection of a urine specimen for culture. The urethra normally contains bacteria in the distal 2 to 3 cm.; hence, the most

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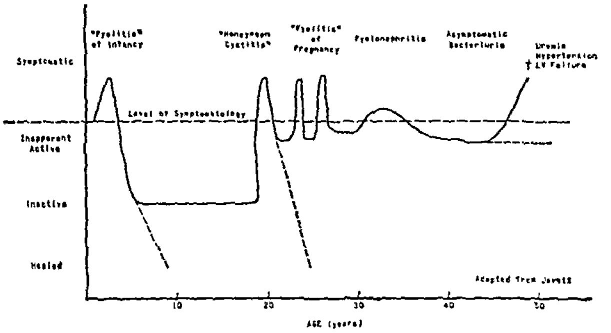
meticulous cleansing techniques cannot avoid contamination with organisms from the urethra either in obtaining voided or catheterized specimens.[6]

The usual method of determining the significance of any given bacterial strain has been the demonstration of its constancy in the urine in the absence of specific therapy. This method has the obvious disadvantage of requiring multiple pretherapy cultures, each taken with meticulous care. The delay this necessitates often cannot be afforded. Recently reemphasis has been placed on various techniques utilizing quantitation of the numbers of bacteria per milliliter of urine to facilitate the differentiation of "significant bacteriuria" from contaminants introduced during collection.[7] The most widely employed technique consists of diluting a fresh or freshly refrigerated urine specimen 1 to 1,000 or more times before inoculating solid culture mediums. Various dilution procedures varying from incorporating tenfold serial dilutions of urine into "pour plates" to streaking medium with a standardized loopful of urine may be utilized. These procedures enable the enumeration of the bacteria per milliliter of urine. We currently use the following technique: 0.1 ml. of urine is pipeted into a tube containing 9.9 ml. of sterile distilled water and the contents well mixed. This gives a 1:100 dilution. Then 0.1 ml. of the 1:100 dilution is added to a Petri dish and covered with approximately 10 ml. of melted cooled nutrient agar. The plate is swirled to effect mixing, allowed to solidify, incubated at 37 C overnight, and the number of bacterial colonies counted. The bacterial count represents the number of bacteria in 0.001 ml. of urine. Such techniques have been shown to be feasible in the routine general hospital laboratory.



Natural history of pyelonephritis illustrated hypothetically. Adapted from Jawetz.[2]

The consensus would place the number which distinguishes significant bacteriuria from contamination in the range of 10,000 to 100,000 bacteria per milliliter of urine. Most specimens which are contaminated during collection contain less than 1,000 bacteria per milliliter, whereas specimens obtained from patients with clinically typical acute pyelonephritis contain greater than 100,000 bacteria per milliliter. While the range between 10,000 and 100,000 bacteria per milliliter seems great, Kass[7c] found only 1% of cultures fell into this range. The relative preponderance of bacterial species isolated changes with the degree of bacteriuria. Coagulase negative staphylococci, of which the majority are nonhemolytic and nonpigmented, are commonly found in cultures with less than 1,000 bacterial colonies per milliliter. Aerobacter aerogenes and Escherichia coli occur more frequently in high concentration. These species are considered to be infrequent contaminants. It should be emphasized that the mere presence or absence of any given micro-organism is not an adequate basis for ruling it in or out as a cause of clinical urinary tract infection. A fairly good correlation exists between the concentration of bacteria and microscopic examination of stained smears of urine. Approximately 5,000 to 10,000 viable bacteria per milliliter have to be present before they can be seen on stained smears.[7b] Kass has reported that staining for bacteria is about 80% reliable.[7c]

Results

By the application of such quantitative techniques to the screening of various groups of patients, significant bacteriuria has been demonstrated with considerable frequency (table 2).[8] The variations in frequency are the result, in part, of the type of patient included in the survey. The incidence of significant bacteriuria was found to be 18% in females and 5% in males with diabetes mellitus, 11% in women at term, 23% in women with cystocoeles, and 70% in men on a urological ward.

The clinical and laboratory features observed in a group of patients with "positive cultures" were compared with those observed in a group of patients with "negative cultures" to ascertain whether or not there were clinical indications suggesting relatively asymptomatic bacteriuria.[3c] These observations were made on 100 consecutive admissions to a female general public medical ward. None of the patients had overt acute pyelonephritis. Urinary tract symptomatology consisting of minimal dysuria, frequency, and nocturia was commonly elicited from patients with positive cultures. Yet these symptoms were not present in all patients with positive cultures and were elicited from a considerable number of patients with negative cultures. Routine urinalyses in each group were quite similar. An attempt was made to separate those with negative cultures from those with positive cultures by noting the combination of clinical observations, such as

Table 1.—*Prognosis of Pyelitis in Infancy*

Author	No. of Patients	Follow-up, Yr.	Abnormalities, %
Wharton and others[3a]..........	30	10	60
Woodruff and Everett[3b]........	76	5-23	40
Macaulay and Sutton[3c].........	27	5	41*

* 5 deaths.

dysuria, frequency, nocturia, and the presence of leukocytes in the urine. Only 1 of 86 patients had this combination in the group with negative cultures; yet only 3 of 14 patients with positive cultures had these findings. It was found that no historical or laboratory evidence allowed separation of patients with positive cultures from those with negative cultures except the quantitative estimation of bacteriuria. Thus, asymptomatic bacteriuria is truly asymptomatic.

Comment

While the over-all incidence of asymptomatic bacteriuria in patients closely approximates the frequency with which pyelonephritis is observed at autopsy, this does not establish a causal relationship and does not answer the question: Is asymptomatic bacteriuria a manifestation of active inapparent pyelonephritis? MacDonald and co-workers [9] recently studied the relationship of bacteriuria to pathological lesions of the urinary tract in 100 unselected autopsies done on adults. The finding of true bacteriuria (defined by them as greater than 100,000 bacteria per milliliter of urine) correlated quite well with the presence of pyelonephritis, and they suggest such a relationship may also obtain during life. Kass [7c] also observed that 40% of patients with asymptomatic bacteriuria during pregnancy will develop apparent acute infection if not given antimicrobial agents. These observations certainly suggest a relationship between asymptomatic bacteriuria and inapparent active pyelonephritis.

It seems apparent that bacteriological study alone can detect these inapparent infections. Bladder catheterization is the commonly accepted technique for obtaining urine from female patients for either examination of the sediment or culture. It has been appreciated that catheterization per se includes some hazard of introducing organisms into the bladder which may be capable of producing urinary tract infections.[10] The incidence of such iatrogenic infection is not precisely known; however, it is probable in 2 to 3% of female patients after catheterization.[11] The disadvantage of this risk must be weighed against overlooking asymptomatic bacteriuria.

Collection of midstream-voided urines combined with quantitative bacterial counting has recently been compared with catheterized urine collections.[12] In a study of 100 consecutive ambulatory and nonambulatory admissions to a female general medical ward "sterile-voided" urine specimens were obtained by ward personnel, which included both graduate and student nurses.[8c] Urine obtained from 61 patients had less than 1,000 bacteria per milliliter, while that from 17 patients contained greater than 100,000 bacteria per milliliter. An "essentially negative" urine culture obtained by voided technique is obviously as meaningful as an "essentially negative" culture obtained by catheterization. Of the 17 patients with large high concentrations of bacteria on voided specimens, 13 had similar numbers of the same bacterial specie on subsequent catheterized specimens.

Kass [7c] has reported that "specimens voided into sterile containers could be obtained from females and from children and used for quantitative study." The correlation between voided specimens with bacterial counts exceeding 100,000 bacteria per milliliter and catheterized specimens is over 95%. The technique of "sterile-voided" urine cultures has been employed routinely at the Boston Lying-In Hospital for the past year and has been found to be feasible as well as satisfactory.[13] Thus, it becomes feasible to screen patients for inapparent pyelonephritis without the risk of introducing infection. However, with preliminary evidence of a significant degree of bacteriuria, either careful repetition of a "sterile-voided" urine collection or catheterization is advisable before undertaking extensive urological or bacteriological diagnostic and therapeutic regimens. Jackson and co-workers [12a] estimate that 5% of patients with low degrees of bacteriuria actually have chronic pyelonephritis. Thus, detection of the abacteriuric phase of inapparent pyelonephritis remains elusive.

TABLE 2.—*Frequency of Asymptomatic Bacteriuria in Hospitalized Patients*

Author	Percentage with Positive Cultures	
	Male	Female
Marple[7a]	...	23
Loopuyt[8a]	3	29
Kass[7c]	12 5*	30 6*
Merritt and Sanford[8c]	...	14
Boshell and Sanford[8b]	...	15

* Outpatients.

Detection of the presence of inapparent pyelonephritis merely opens the door to many important questions to be answered. Are such patients predisposed to subsequent acute apparent infections? Does inapparent pyelonephritis progress to subsequent chronic pyelonephritis with hypertension and renal insufficiency? Does therapy alter the course of inapparent pyelonephritis? Most of these as yet are unanswered. In preliminary observations, Kass [7c] noted that if bacteriuria were eliminated during pregnancy, acute pyelonephritis was not encountered; whereas about 50% of patients with bacteriuria treated with placebo during pregnancy developed overt infection.

Summary

The discrepancy noted between the incidence of significant pyelonephritis demonstrable at autopsy examination and the antemortem diagnosis of pyelonephritis suggests the existence of inapparent

pyelonephritis as a phase in the natural history of pyelonephritis. The over-all incidence of "asymptomatic bacteriuria" fairly closely approximates the frequency with which pyelonephritis is observed at autopsy. Evaluation of asymptomatic bacteriuria is dependent upon bacteriological quantitative estimation of bacteriuria. Clinical history or urinalysis does not aid in detection of bacteriuria. The utilization of a quantitative culture technique enables satisfactory evaluation of voided urine cultures obtained from female patients. This facilitates detection of inapparent infection by eliminating the hazard of introducing infection. The role of inapparent pyelonephritis in the genesis of chronic pyelonephritis and the effect of therapy in altering the course of inapparent pyelonephritis is still unknown.

5323 Harry Hines Blvd. (19).

Drs. B. Boshell, C. B. Favour, J. H. Harrison, and A. D. Merritt and Mrs. F. H. Mao assisted in various phases of these studies.

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MUTAGENIC AGENTS.—Perhaps it will eventually be recognized as one of the most significant medical features of the early 20th century that, as a by-product of more and more powerful therapeutic procedures and the production of chemical substances outside biologic experiences, the normal protective barriers that kept mutagenic agents from the internal organs have been more and more frequently penetrated. Ionizing radiation is the most important, but . . . other agents must be at work, with increasing leukaemic incidence as the only evidence as yet of their presence. It may be only a tiny price that has to be paid for the advantages of a scientific civilization, but it is disquieting and it raises the lurking fear that anything that is increasing the incidence of leukaemia may also be breaking through the other barriers that in the past have protected the germ cells from mutagens. I think one would be wise to pay more attention to leukaemia even than its intrinsic interest and lethality demand just because of the possibility that it is the best indicator one can have of the last and greatest danger to civilization, active and avoidable genetic deterioration. . . . The exposure to physical and chemical mutagens should be reduced as much as possible. This in its turn calls for the recognition of the significant mutagenic agents in an environment always being modified by scientific and technologic development. The importance of ionizing radiation has now been recognized, and one knows how one should act in regard to it. On the chemical side a beginning has hardly been made.—M. Burnet, Leukaemia as a Problem in Preventive Medicine, *South African Practitioner*, January, 1959.

PRACTICAL VALUE OF ANALYSIS OF URINARY CALCULI

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Classification of urinary calculi depends on comparatively simple chemical tests. Such tests yield valuable clues as to the cause of the lithiasis and the aim of treatment. The pH of urine normally fluctuates daily over a range from pH 4.5 to 7.5. Isohydruria, a narrowing of the range of diurnal fluctuation, is one of the possible causes of lithiasis and is easily remedied by diet and drugs. The list of other possible causes includes a number of conditions that are easily remedied once the cause is identified.

Urinary calculi should be analyzed after their removal or passage from the urinary tract in order to properly manage the future of the patient. Knowing the chemical composition of the calculus gives important information as to what substances are coming down in the urine and gives clues to any causes of recurrent stone formation which may be present. Although this same information may be deduced by other means, such as studies of urinary sediment, blood and urine chemistry studies, urine and blood pH records, and urologic x-ray investigation, the chemical analysis of the stone may give the first exact information and confirms the other studies.

Analysis and Chemical Composition

Analysis.—The four common crystalloid compounds in urinary stones[1] are calcium phosphate, calcium oxalate, magnesium ammonium phosphate, and uric acid; less common are calcium carbonate and cystine stones. Mixtures of these salts are common. Sulfonamide calculi are now rare. Many subtypes of common calculi due to variations in physical and chemical structure and many rare constituents are found by petrographic methods of analysis,[2] such as polarized microscopy (spectrography), x-ray crystallography, x-ray microdiffraction, microradiography, and paper chromatography. Traces of bismuth, copper, zinc, lead, silver, manganese, and fluorine have been found. As yet, these biophysical methods and findings are not practical in clinical management of the patient with urinary calculi. The presence of the common crystalloids may be determined by using eight simple spot tests (see table).

Chemical Composition.—The findings of these qualitative tests indicate the compounds which make up the stone. Uric acid and cystine stones are usually pure. Calcium is combined with phosphate, oxalate, or carbonate. A combination of magnesium and ammonium and calcium phosphate (triple phosphate) is found in infected urine. Chemical composition may direct attention to some of the exogenous and endogenous influences on the absorption, excretion, and precipitation of the crystalloids. This can be associated with knowledge of the mechanisms of stone formation.

Mechanism of Stone Formation

The urinary crystalloids are present in a supersaturated solution of electrolytes and nonelectrolytes controlled by presence of suspended colloids which also maintain a surface tension equilibrium with the urinary tract mucosa.[3]

Although there is constant crystallization and resolution of crystalloids, any disturbance of the surface tension equilibrium of the crystalloid-colloid interface or the urine-mucosa interface may cause a precipitation and conglomeration of mucopolysaccharides and mucoprotein nidus or matrix covering and preventing resolution of precipitated crystalloids. A formula of normal equilibrium and a formula of stone formation is as follows:

$$\text{Crystalloids} \longleftrightarrow \text{colloid} \longleftrightarrow \text{mucosa} \qquad \xleftrightarrow{\text{equilibrium}} \qquad \text{no stones}$$

$$\underset{\hookrightarrow}{\text{Crystalloid precipitate}} + \underset{\hookrightarrow}{\text{colloid precipitate}} \qquad \underset{\longrightarrow}{\xleftrightarrow[\text{equilibrium}]{\text{loss of}}} \qquad \text{stone formation}$$

The known exogenous and endogenous causes of stone formation affect the equilibrium at various points of the formula. They are frequently interrelated. The seven types of tendencies to calculus formation are as follows: (1) metabolic disturbances (anabolic and catabolic), uricaciduria (gout, polycythemia), oxaluria, and cystinuria; (2) endocrinopathy: hyperparathyroidism; (3) urinary obstruction (stasis): hydronephrosis; (4) infection: urea-splitting bacteria; (5) mucosal metaplasia: avitaminosis A; dietary deficiency; Randall's plaques; (6) extrinsic: dehydration; dietary excess (milk drinkers); drug excess (alkalizers, purine drugs); recumbency; chemotherapy; and (7) isohydruria[5]: loss of wide acid-alkaline tides and fixation of urinary pH. Although any one of these disturbances may be present without the formation of calculi, two or more are associated with most instances of stone formation, and the isohydruria is the condition most often found in combination with the others.

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Read before the Joint Meeting of the Section on Pathology and Physiology and the Section on Urology at the 107th Annual Meeting of the American Medical Association, San Francisco, June 26, 1958.

Isohydruria is the fixation of urinary pH within a narrow range throughout most of each 24-hour cycle instead of a normal, widely fluctuating acid-alkaline tide (pH 4.5 to pH 7.5). The pH figures as noted on nitrazine paper have been practical for clinical use. Bridges and Mattice [4] have shown that the diurnal acid-alkaline pH curve follows as regular an individual specific pattern as do human fingerprints. During stone formation, there is fixation of pH levels with characteristic but only mild fluctuations of that individual's normal curve. Reynolds [5] suggested the term "isohydruria" for this condition whether it be in the acid, alkaline, or neutral range. Isohydruria of acid type (pH 4.5 to 5.5) is associated with uric acid precipitation; alkaline isohydruria (pH 7.0 to 7.5) promotes precipitation of calcium phosphate calculi; and mildly acid to neutral fixation (pH 5.5 to 6.0) favors calcium oxalate stones.

*Spot Tests to Determine Presence of Common Crystalloids in Urinary Calculi**

Chemical	Method	Finding
1. Uric acid	Powdered stone; 1 drop 20% sodium carbonate; 2 drops uric acid reagent	Prompt deep blue color (pale blue is negative)
2. Phosphate	Powdered stone†; 4-5 drops ammonium molybdate (3.5 Gm. in 75 cc. water and 25 cc. concentrated nitric acid)	Distinct yellow precipitate (may be warmed)
3 Oxalate	a. Powdered stone; 2-3 drops 10% HCl; if no effervescence, cool and add pinch of manganese dioxide; do not mix	Tiny bubbles of gas explosively released from bottom
	b. Char small fragment on spatula and add 2 drops 10% HCl‡	Foaming effervescence
4. Carbonate	relatively large sample of powdered stone; 8-10 drops 10% HCl (save for 5, 6, 7a)	Foaming effervescence
5. Calcium	Acid extract§; 2-3 drops 20% NaOH	Fine white precipitate or film from oxalate stones; dense precipitate from phosphate stone
6. Magnesium	Acid extract; 2-3 drops of 20% NaOH; 2-3 drops "M" (ρ-nitrobenzene-azoresorcinol, 1 mg. in 100 cc. normal NaOH)	[illegible] forms)
7. Ammonium	a. Acid extract; 2-3 drops of 20% NaOH; 2-3 drops Nessler's solution	Yellowish orange precipitate
	b. powdered stone; 2-3 drops Nessler's solution	Yellowish orange precipitate
8. Cystine	a. Powdered stone; 1 drop NH_4OH; 1 drop 5% NaCN (wait 5 minutes); 2-3 drops 5% sodium nitroprusside	Beet-red color; on standing may fade to orange-red
	b. Char over flame‡	Hydrogen-sulfide odor

* Adapted from Winer and Mattice.[1]

† Performed on a micro slide, it is much easier to see the precipitate. (The other tests are best performed on an artist's spot plate on which several calculi can be analyzed simultaneously.)

‡ Simple alternate methods require heat to char the stone fragment in a platinum spatula. Technical errors can be avoided by washing surface and taking samples by scraping various layers and nucleus with a knife.

§ With use of a medicine dropper, tip plugged with a wisp of cotton, acid extract from no. 4 is taken up, cotton removed, and filtrate divided for nos. 5, 6, and 7.

Isohydruria is only a single factor influencing precipitation of the crystalloids and their colloid matrix by disturbance of equilibrium at colloid-crystalloid interface. Isohydruria may be of intrarenal origin (excretory enzymes, electrolyte excretion) or may be due to extrarenal causes, such as stasis or infection (residual urine prevents widely changing pH as a hydronephrosis and vesical neck obstruction. Infection may give a constant alkaline pH fixation). Isohydruria has been found to be temporary in some patients and permanent in others. The permanent types usually show pure calculi, whereas the temporary types often show mixed types of calculi and will on occasion have wider fluctuations of pH.

Components of Calculi

Considerable information is known regarding absorption, excretion, and precipitation of crystalloids in calculi.[6] Further investigation of the colloid factors may yield practical tests of chemical significance in the future, but only the crystalloid factors have practical clinical significance at this time.[7]

Calcium.—Although the diet contains both organic and inorganic calcium, only inorganic calcium is absorbed, probably in the upper small intestine. Calcium absorption is improved by an acid reaction and enhanced by digestion of sugars which produce intestinal acidity. Vitamin D increases calcium absorption. Dietary fat lessens calcium absorption in a high-calcium, low-phosphorus diet, but calcium absorption is increased by dietary fat with a low-calcium, high-phosphorus diet. Calcium chloride, calcium lactate, and calcium gluconate are soluble and easily absorbed, whereas the phosphate is poorly soluble and resists absorption. Protein increases calcium absorption by forming soluble calcium-amino acid complexes.

Milk and cheese are the most important calcium-containing foods. Hard water and some vegetables, especially carrots, have readily absorbable calcium, whereas spinach, rhubarb, and other high oxalate vegetables diminish calcium absorption.

Calcium is excreted into the lower small intestine and into the urine. About 150 mg. of calcium are excreted daily in the urine, but this varies widely even with a fixed diet. A positive "calcium balance" occurs when the quantity of calcium absorbed is greater than the amount excreted in the urine and bowel, occurring during growth, pregnancy, after calcium starvation, or after testosterone administration. Negative calcium balance occurs in rickets, sprue, osteomalacia, and hyperparathyroidism, during starvation, and with prolonged recumbency.

Phosphorus.—Normal urinary phosphorus occurs mostly as sodium phosphate, some as potassium phosphate, and less as calcium and magnesium phosphates; the latter salts precipitate in alkaline urine. Ingestion of alkali may cause cloudy urine (phosphaturia) by facilitating the precipitation of insoluble calcium and magnesium phosphates. The levels of urinary phosphates increase during starvation, during severe muscular exercise, and after the administration of a high-protein diet, calcium and ammonium chlorides, or parathyroid extract (Parathormone). The urinary phosphate levels diminish during pregnancy, alkalosis, renal insufficiency, and tetany and with certain bone diseases.

Calcium Phosphate Calculi.—Calcium phosphate calculi occur with excess milk intake, excess alkali intake (ulcer therapy), stasis, recumbency, avitaminosis A, hypervitaminosis D, isohydruria of a moderately alkaline type, and dehydration. In the presence of urea-splitting bacterial infection, mixed calcium phosphate and magnesium ammonium phosphate calculi occur.

Calcium phosphate calculi are associated with bone disease.[8] Hyperparathyroidism (generalized osteitis fibrosa cystica) shows hypercalciuria with precipitation of insoluble calcium phosphate in the renal pelvis, the renal parenchyma, and the other acid-excreting tissues (stomach and lungs). In osteitis deformans (Paget's disease of bone) 10% of patients have calculi. Osteoporosis with hypercalciuria occurs in the postmenopausal state, especially after surgical castration. Such hypercalciuria also is seen in senility, disuse atrophy, and decalcification of immobilization, treatment with estrogens, malnutrition, Cushing's syndrome (rare), ACTH treatment, cortisone treatment, acromegaly, multiple myeloma, hypervitaminosis C, and Fanconi syndrome (aminoaciduria).

Oxalates.—Oxalates are normally present in the urine and blood. Reliable methods of determination of blood-oxalate levels are not generally available. The normal urinary oxalate is 20 to 47 mg. in 24 hours. Urinary oxalate is supersaturated from two and one-half to three and one-half times its normal solubility at pH 5.5.[9]

Blood oxalate develops from dietary oxalate absorption, from oxalate formed by bacterial activity in the intestine, and as an intermediate product during endogenous tissue metabolism. Urinary oxalate excretion persists on an oxalate-free diet and during starvation. Spinach, rhubarb, and asparagus contain large amounts of oxalate, and many of the common fruits and vegetables have it in smaller amounts. The oxalate may be present as insoluble calcium oxalate, as soluble sodium and potassium oxalates, and, in very slight amounts, as oxalic acid. Hyperchlorhydria increases and achlorhydria decreases oxalate absorption. The soluble oxalate in the food may be absorbed; milk, with its high calcium content, prevents absorption of soluble dietary oxalates by converting them into insoluble calcium oxalate.

Tissue glycogen is a probable source of oxalic acid; oxalates are produced when carbohydrates are incompletely metabolized as in diabetes and liver disease. Oxalates may also result from the digestion of the proteins and fat. Although the oxalic acid is relatively inadequately traced in endogenous metabolism, studies show that administration of glucose, ethylene glycol, glyoxal, and glycolic acid increase oxalic acid in the urine. (Mandelic acid splits into phenol or glycocolic acid, the latter being a precursor of oxalic acid.)

Calcium oxalate calculi occur with oxaluria due to dietary excess, possible dietary deficiencies, possible metabolic errors, isohydruria at pH 5.5 to 6.0, associated with hypercalciuria, stasis, and dehydration. Oxalate metabolism and stone formation are poorly known mechanisms. Oxalate calculus formation due to acetazolamide (Diamox) has been noted, the carbonic anhydrase inhibition causing fixation of urine pH. Oxalate calculi are formed frequently with Boeck's sarcoid.

Hammarsten [10] believes that endogenous oxalate is an undesired by-product due to a metabolic disturbance resulting from magnesium deficiency. High levels of urinary magnesium are said to increase calcium oxalate solubility. In 1937, Hammarsten produced oxalate stones in rats with a low magnesium diet; the stones were larger and more numerous in the absence of vitamins and a diminution of calcium in the diet caused an increased elimination of calcium in the urine; this was more marked when the animal was deficient in vitamin D, thereby lowering absorption of calcium from the intestine. She believed that under such circumstances calcium is mobilized from the bones in excess of requirements, the excess being excreted in the urine. Stones were formed even if the diet was free of oxalate, but additional oxalate in the diet caused an increase in stone formation. The highest incidence of oxalate stones occurred with a low magnesium, high oxalate, low vitamin, acid ash diet. The resulting acid-sterile urine showed a decreased magnesium content and an increase of calcium oxalate calculi. If the diet was of alkaline ash type, calcium phosphate calculi were produced.

Uric Acid.—Exogenous uric acid is derived from dietary purines, while the endogenous portion is derived from the degradation of nucleoproteins during tissue catabolism, as well as from free mononucleotides found in muscles and glands. The liver is the probable site of destruction of 30 to 70% of the uric acid production, the remaining being excreted in the urine as free uric acid and as sodium potassium and ammonium urates. The output of urinary uric acid is 0.5 to 1.0 Gm. per 24 hours.

Uric acid calculi are usually pure (rarely urates) and are found with uricosuria, hyperuricemia, mild polycythemia (which is noted in many patients with uric acid calculi and uric acid showers), polycythemia vera, stress polycythemia,[11] lymphomas (without and especially with treatment), exogenous dietary excess, or purine drug therapy (theophylline), acid isohydruria, and hepatic disease. Relatively more bladder stones are of uric acid composition than are kidney stones. However, uric acid kidney stones may elude diagnosis and removal due to their radiotranslucency.

Comment

After a calculus is obtained from the patient, it is important to eliminate any known causes of stone formation. Chemical analysis may give information as to the specific causes of formation of each type of stone and as a guide to preventing further precipitation of this compound in the urine.

Attempts should be made to prevent excessive absorption, endogenous formation, concentrated excretion and diminished solubility. Where the etiology is unknown, the chemical composition indicates the type of isohydruria which permits each particular crystalloid to be precipitated with its associated matrix. Isohydruria may be changed by proper utilization of drug and dietary means. Intermittent alkalinization may be achieved through use of palatable alkalis or alkaline ash foods (cantaloupe is the food of greatest effect). Intermittent acidification is achieved with sodium acid phosphate, ammonium chloride, betaine hydrochloride, or acid ash foods. Cranberry juice was found to be the most potent dietary acidifier in a study of a group of paraplegics with urinary calculi. The occasional need for rapid diuresis led to use of various diuretics, but beer gave an adequate rapid diuresis in most cases.

Summary

Simple spot-test chemical analysis of urinary stones gives practical information of value for management of the patient with urinary calculi.

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FIBRINOLYSIS IN UROLOGIC PATIENTS

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Severe hemorrhages after prostatic surgery may be due to a fibrin-dissolving protease found in normal prostatic tissue. The intravascular release of enzyme activators from the prostate may also explain the chronic fibrinolysis that occurs in metastatic carcinoma of the prostate. Experiments in vitro showed that the activity of these enzymes can be opposed by inhibitors. The effectiveness of two preparations of toluidine blue as inhibitors was convincingly shown by observations of plasma fibrinogen levels in 3 groups of 30 patients undergoing prostatectomy. One group received an oral preparation, the second, a parenteral preparation. The third group served for comparison. Liquefaction of extravasated blood in the prostatic fossa was found to be a characteristic phenomenon, but the question is raised whether this may be an essential part of some reparative process. Two case histories illustrate the occurrence and treatment of hemorrhage after prostatectomy.

Acquired fibrinogenopenic states occur rarely in urologic practice. It is perhaps for this reason that this hemorrhagic diathesis has not been recognized more frequently. Most physicians agree that fibrinolysis is associated with urologic cases of hypofibrinogenemia. The fibrinolytic systems, when completely understood, will probably rival in complexity the process of blood coagulation.

A proteolytic enzyme system is present in human plasma (fig. 1). Active enzyme can be prepared from the globulin fraction and an inhibitor from the albumin. The active enzyme plasmin (fibrinolysin) will act on a variety of such substrates as fibrin, fibrinogen, thrombin, prothrombin, casein, and gelatin. Since the enzyme system is not fastidious, it is frequently classified as proteolytic rather than fibrinolytic. The enzyme is derived from a precursor, plasminogen (profibrinolysin). The conversion of plasminogen to plasmin may be caused by the alarm reaction with such stress as severe physical trauma, shock, hemorrhage, burns, and fear. Plasminogen

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may be activated as a result of release into the circulation of tissue activator substance and by the activity of bacteria.

A proteolytic enzyme is present in normal prostatic tissue. Tagnon and associates[1] first reported the presence of this fibrinolysin. These investigators considered this to be the fibrinolytic enzyme originally described as present in the prostatic fluid by Huggins and Vail.[2] This fibrinolysin is similar in action but probably not identical to the plasmin in normal serum.

It may be postulated that fibrinolysis associated with prostatic surgery or the chronic fibrinolysis occurring in metastatic carcinoma of the prostate may be entirely due to intravascular release of the prostatic proteolytic enzyme or due to intravascular release of enzyme activators from the prostate triggering the plasmin system. The pathogenesis in prostatic surgery may conceivably be the general alarm reaction with subsequent activation of plasminogen. It is possible that both the plasmin and prostatic systems are activated.

Studies

The fibrinolytic activity of the prostatic enzyme can be demonstrated in vitro by the fibrin plate method.[3] Purified bovine or human fibrinogen placed on Petri dishes is converted to fibrin by the addition of thrombin. Drops of test preparations are placed on the fibrin plates. Lysis produces a spreading zone of liquefaction, and the area of this, related to time, gives a quantitative measurement. Unheated fibrin plates contain plasminogen as a contaminant and thus are lysed by plasminogen-activators, such as tissue kinases. Plasminogen in such plates may be destroyed by heat denaturation.[4] The zone of liquefaction produced on a heated fibrin plate by an extract of prostatic tissue therefore represents lysis by the prostatic enzyme.

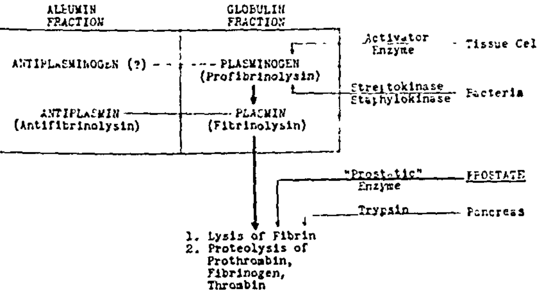

Fig. 1.—Schema of proteolytic enzymes.

Figure 2 shows a heated fibrin plate incubated with benign prostatic tissue. An extract of malignant prostatic tissue incubated on a heat-denatured fibrin plate gives a larger zone of liquefaction, indicating greater fibrinolytic activity (fig. 3).

In vitro studies were undertaken to find inhibitors of the prostatic fibrinolytic enzyme. Two inhibitors were found to be effective in fibrin plate tests, toluidine blue and Klot. Klot is a parenteral preparation of 7% *n*-butyl alcohol with 0.002% toluidine blue in isotonic sodium chloride solution. A test drop of malignant prostatic tissue incubated on a heated fibrin plate prepared with toluidine blue liquefied a small zone of fibrin (fig. 4). The small zone of dissolution indicates inhibition of lysis. A heated fibrin plate prepared with the addition of Klot was incubated with malignant prostatic tissue (fig. 5). A small zone of liquefaction indicates inhibition of lysis.

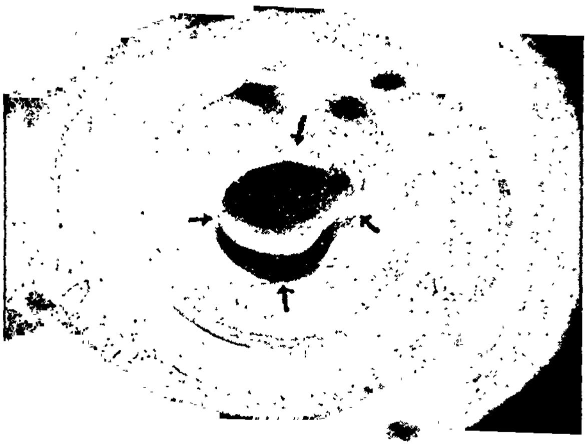

Fig. 2.—Heat-denatured fibrin plate incubated with extract of benign prostatic tissue, showing zone of lysis.

In acute cases of the prostatic fibrinolytic diathesis, the proteolytic enzyme acts to destroy fibrinogen, accelerator globulin, and prothrombin. A clinical survey was undertaken to evaluate the fibrinogen levels during transurethral prostatectomy. Plasma fibrinogen levels were determined preoperatively and one hour and four hours postoperatively in three groups of 30 patients having transurethral prostatectomies. The first group, the controls, received no special medicaments; the second group received 200 mg. of Blutene, an orally given toluidine blue preparation, 12 hours before surgery; and the third group was given Klot intravenously at the start of resection in a dosage of 1 ml. per 15 lb. of body weight. There were five cases of malignant prostatic carcinoma in each of the three groups.

In the control group the average drop in fibrinogen level from the preoperative period to four hours postoperatively was 20.3%, in the toluidine blue group 11.2%, and in the Klot group 6.3%. More striking is the observation that in 6 of the 30 subjects in the control group the fibrinogen level dropped below the low of accepted normal, 250 mg.%. In one of the six it dropped to zero, or afibrinogenemia. In the groups treated with toluidine blue and Klot, none of the fibrinogen levels postoperatively were below normal.

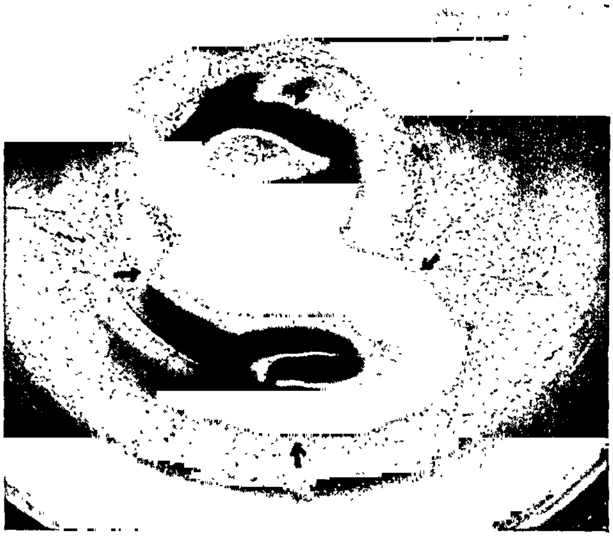

Fig. 3.—Heat-denatured fibrin plate incubated with extract of malignant prostatic tissue, showing large zone of lysis.

In recent studies, I have attempted to study the fibrinolytic activity of the prostatic fossa after prostatectomy. I thought that prostatic fibrinolysin may cause delayed or secondary hemorrhage by the premature dissolution of hemostatic blood clots before permanent repairs occur. Such hemorrhages would be postulated to occur more frequently after transurethral resection of adenocarcinoma of the prostate, since malignant prostatic tissue shows greater lytic activity. The problem of postprostatectomy hemostasis and hemorrhage is not limited to transurethral resections of carcinoma of the prostate. Conceivably, clot dissolution may occur after enucleation of a benign adenoma.

Figure 6 illustrates the method of collection of blood from the prostatic fossa after prostatectomy. A three-way urethral catheter is employed postoperatively. The catheter's irrigating lumen is plugged at the catheter tip and a hole made in the irrigating channel proximal to the retention balloon at a position corresponding to the prostatic fossa. Blood may be suctioned from the prostatic fossa postoperatively through this revised irrigating channel. There has been considerable variation in the amount of blood aspirated from the prostatic fossa. During periods of collection for blood determinations and evaluation of lytic activity, mild traction has been placed on the catheter to seat the catheter balloon against the bladder neck. This avoids contamination of collections by urine. Blood hematocrit value and hematocrit value of the collected fossa blood are determined for comparison to assure that dilution by urine of the fossa blood has not occurred.

In a group of five patients subjected to suprapubic prostatectomy, fibrinolytic activity was present in three immediately after operation. No clotting of the fossa blood was observed, and in all no fibrinogen was detectable. Lysis was demonstrated in three cases by the fibrin plate test and the lysis time of thrombin-clotted plasma. Complete lysis of blood plasma by fossa plasma in a thrombin-clotted system occurred in 24 hours. In a second group of five patients subjected to suprapubic prostatectomy and treated preoperatively with toluidine blue, no fibrinolytic activity was detected. Accurate fossa fibrinogen level determinations were not possible because of blood clots in the samples. Fibrinolytic activity was not present in the general circulation of these cases.

With present knowledge it is difficult to assess whether this fibrinolytic activity localized to the prostatic fossa is of physiological or pathological significance. Liquefaction of clotted blood is known to occur early in closed spaces, such as hematoceles and hemothorax. Alteration of this possibly physiological proteolytic activity in the prostatic fossa may be detrimental to normal healing.

Report of Cases

The cases of acute fibrinolysis observed on the urologic service have occurred mainly during or after transurethral resection. Fibrinolysis has been observed in resections of benign and malignant prostates. This hemorrhagic diathesis has occurred in resections of unsuspected malignant prostates, known malignant prostates without previous hormonal therapy, and known malignant prostates

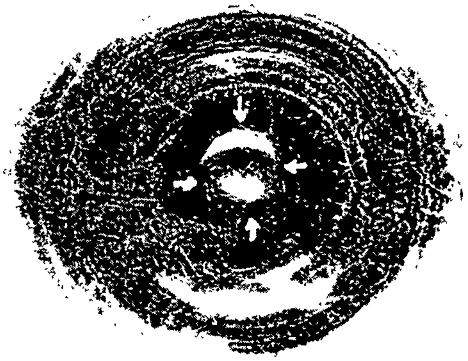

Fig. 4.—Heat-denatured fibrin plate prepared with toluidine blue and incubated with malignant prostatic tissue, showing inhibition of lysis.

during adequate hormonal therapy. Chronic fibrinolysis or instances in which fibrinolysis proceeds slowly has been observed in disseminated prostatic and bladder carcinoma.

The following case demonstrated acute fibrinolysis after transurethral resection of malignant prostatic carcinoma while the patient was on hormonal therapy.

Case 1.—A 76-year-old man entered the hospital because of symptoms of urinary obstruction. Twelve years preceding admission a transurethral resection of the prostate was performed for obstructing adenocarcinoma of the prostate. The patient had been maintained on estrogen therapy for the 12 years. On examination the testicles were atrophic and the prostate small and clinically malignant. An x-ray survey of the bones revealed no evidence of metastases. The serum acid phosphatase level was 6.7 King-Armstrong units. A transurethral resection of the prostate was performed without incident. Four hours postoperatively profuse bleeding from the catheter, without clots, was noted. The blood-clotting time was five minutes, and complete lysis of the clot occurred in one hour. The plasma fibrinogen level was 39 mg.%. Five units of whole blood, 5 Gm. of fibrinogen, and 20 ml. of Klot were administered. Nine hours postoperatively the hemorrhage was controlled. The next day, the blood-clotting time was 5 minutes and there was no clot lysis in 24 hours. The patient was discharged on the sixth postoperative day.

The following patient showed acute fibrinolysis after transurethral resection of benign prostatic tissue.

Case 2.—A 56-year-old man was admitted to the hospital because of symptoms of urinary obstruction. Early during transurethral resection of the prostate the capsule was perforated. The surgeon completed the resection while bleeding continued from the site of perforation. A total of 19 Gm. of benign prostatic tissue was resected. The estimated blood loss at surgery was 800 ml. The patient returned to his room with a stable blood pressure with whole blood being given intravenously. One hour postoperatively profuse bleeding from the catheter, without clots, was noted. Subcutaneous hemorrhages developed on both upper extremities. The blood-clotting time was six minutes, and there was complete clot lysis in two hours. The plasma fibrinogen level was 100 mg.%, and the platelet count was normal. Therapy included 4 units of whole blood, 2 Gm. of fibrinogen, and 25 ml. of Klot given intravenously. Eight hours postoperatively the bleeding was controlled, the plasma fibrinogen level was 220 mg.%, and no clot lysis was observed in 24 hours.

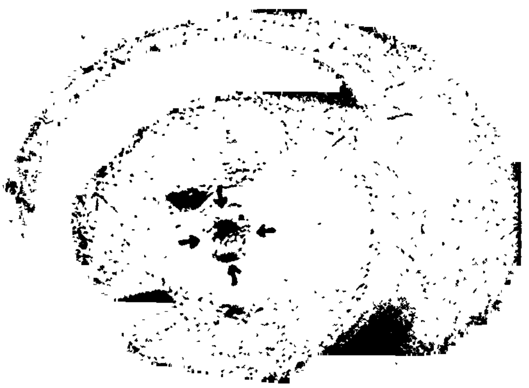

Fig. 5.—Heat-denatured fibrin plate prepared with Klot and incubated with malignant prostatic tissue, showing inhibition of lysis.

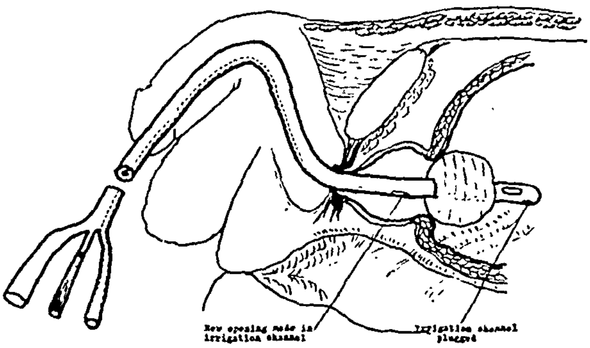
New opening made in irrigation channel
Irrigation channel plugged

Fig. 6.—Method of collecting blood from prostatic fossa after prostatectomy with revised continuous irrigation catheter.

Diagnosis

The first requisite for establishing the diagnosis of fibrinolysis as a cause of abnormal bleeding is the consideration of its possible existence. Generalized ooze may be noted in the prostatic fossa during transurethral resection. I have noted the delayed occurrence of the lytic syndrome up to six hours postoperatively. Bleeding via the urethral catheter may suddenly change from pinkish or dark old blood to bright red drainage. Usually the bright red blood from the catheter is without blood clots. Sites of fresh punctures in the skin for medication bleed profusely. The skin puncture for spinal or caudal anesthesia may bleed. Subcutaneous and submucosal hemorrhages are noted.

There are many methods of studying fibrinolysis. From the point of view of the clinician, observation of the blood clotting and the future integrity of the clot is both a diagnostic test and also helpful in following the effectiveness of therapy. Venous blood is allowed to clot in a glass test tube at 37 C. The clot is observed from time to time. If lysis occurs, the red blood cells become free and sink to the bottom of the tube, leaving a top layer of serum. In severe cases, the clot may lyse very rapidly after clotting of blood or there may even be no clot formation whatever. The activity of the fibrinolytic enzyme is in direct proportion to the time required for the lysis of the clot.

It is important to remember that clot lysis may be more apparent than real in hypofibrinogenemia. Blood which has a very low concentration of fibrinogen forms a temporary solid clot which is unable to hold together the mass of red blood cells as it retracts. The small retracted mass of fibrin that ultimately remains is masked by a mass of cells, thus making it appear that liquefaction of the whole clot has occurred. Fibrinogen level and prothrombin time determinations and a platelet count are helpful in establishing an accurate diagnosis.

Treatment

In acute fibrinolysis immediate and vigorous measures must be taken. Shock may result in massive activation of fibrinolysin. With further destruction of coagulation proteins, more bleeding takes place and the shock state deepens. Death results unless such a vicious cycle is interrupted. Reference to figure 1 helps to understand the rationale of therapy. Whole blood is essential for rapid replacement and maintenance of blood volume. Whole blood acts upon the abnormal plasma proteolytic activity both directly and indirectly. The direct action is in the supplementation of the patient's plasma with the antifibrinolysin of the albumin fraction. A disadvantage of whole blood is its normal content of profibrinolysin and fibrinolysin of the globulin fraction. With more profibrinolysin available to the patient's enzyme activating system, the proteolytic activity is augmented. The indirect action of whole blood on fibrinolysis is in the supplementation of substrate in the form of fibrinogen, prothrombin, and other coagulation factors. The prevention of shock is probably the most important single indication for blood transfusions in acute fibrinolysis.

Administration of human serum albumin is a direct attack, for it is in the albumin fraction of blood that antifibrinolysin resides. Fibrinogen supplies large amounts of substrate to expend the lytic enzyme and also restores the clotting mechanism. I have alternated 1 Gm. of fibrinogen and 100 ml. of albumin every half hour until there is clinical lessening of bleeding.

Toluidine blue or Klot has been given intravenously for inhibition of circulating lysin. The dosage of toluidine blue found effective is 100 mg. and of Klot 1 ml. per 15 lb. of body weight. Toluidine blue must be diluted to 100 ml. in a vehicle such as glucose and water.

Stefanini and Gendel[5] have reported satisfactory control of the bleeding tendency of disseminated prostatic carcinoma by the administration intramuscularly of ACTH (80-120 units daily in divided doses) or cortisone (150-200 mg. daily in divided doses) until bleeding is arrested. The chronic fibrinolysis of disseminated prostatic carcinoma can often be controlled by stilbestrol therapy. As remission sets in and dissemination of the prostatic tissue is reduced, the bleeding tendency regresses and fibrinolysis disappears.

Comment

It is probable that fibrinolytic activity developing spontaneously in patients who have undergone transurethral resection is due to release into the blood stream of prostatic proteolytic enzyme. Further resection, with open venous sinuses or capsular perforation, provides possible sites for entry into the circulation of prostatic proteolytic enzymes or prostatic tissue activators to trigger the plasma enzyme system. Further evidence for this is the observation that men undergoing transurethral resection of bladder tumors maintain essentially constant plasma fibrinogen levels in the postoperative period. A possible deduction from this is that manipulation or massage of the prostate by a sheath riding over the prostate is not sufficient for intravascular release of prostatic proteolytic activators or enzymes. Further studies of localized prostatic fossa fibrinolytic activity may lead to remedies of the problem of postprostatectomy bleeding and secondary hemorrhages.

Summary

Fibrinolysis in prostatic surgery may be due to intravascular release of the prostatic proteolytic enzyme or of enzyme activators from the prostate triggering the plasmin system. Two prostatic fibrinolytic enzyme inhibitors, toluidine blue and Klot (a parenteral preparation of 7% *n*-butyl alcohol with 0.002% toluidine blue in isotonic sodium chloride solution), were found effective in in vitro and in vivo studies. Acute fibrinolysis after transurethral resection was demonstrated in two surgical patients, one with benign prostatic tissue and one with malignant prostatic carcinoma while on hormonal therapy. Observation of the blood clotting and the subsequent integrity of the clot is a diagnostic test and is also helpful in following the effectiveness of therapy. In acute fibrinolysis, immediate and vigorous measures must be taken.

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The toluidine blue (Blutene) used in this study was supplied by Abbott Laboratories, North Chicago, Ill. Klot, hemostatic injection, code 71A-47, was supplied by the Warren-Teed Products Company, Columbus, Ohio.

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PLANNED DEVELOPMENT OF LATENT ANAL SPHINCTER

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This presentation has for its object the demonstration of a plan to accomplish the reconstruction and development of a workable anal sphincter, many years after birth, for patients born with imperforate anus and helped at the time of birth by colostomy. As the plan unfolds it will be seen to involve a composite concept of the embryology, the myoneural mechanism latent in the anal plate, reconstructive surgery, a highly disciplined regimen of muscle exercises in conjunction with counter-pressures, and finally the restoration of bowel continuity and abolition of the colostomy. The principles may be applied in other situations.

The first case of an attempt of this kind was reported in The Journal in 1951.[1] As a progress note on that case it is to be noted that since the definitive surgery in 1949, the patient has had no dilatations and no dietary restrictions and fully controls his bowel movements. He is happily married and has a family; he is fully employed and carries standard rate life insurance. In short, he leads a normal life.

The present case, however, presented a slightly different problem. As a result of the encouragement and experience gained from the first case, I believe the present plan to be an improvement.

Report of a Case

On June 18, 1951, a father brought his 12-year-old son for examination and opinion. The complaint was a permanent colostomy and foul-smelling anal sinus.

History.—The patient was born May 12, 1939, and weighed 3,856 Gm. (8.5 lb.); delivery was normal. Immediately it was noted that he had a totally imperforate anus, probably a Ladd type 3,[2] but there could be located a dimple of faint outline. Within two hours, through this dimple, a surgical opening was made and dilatation was done. In spite of strong laxatives, enemas, and repeated dilatations he remained at all times very constipated. Stricture was thought to be the problem, but by 9 years of age, when fecal impaction reached the splenic flexure, a colostomy was necessary. He was considered to possibly have a megacolon (Hirschsprung's disease).

The colostomy was of the double-barreled type. It brought new problems, although it saved the patient's life. In the first 11 years of his life he had had 11 major operations, the first series having been directed at the anal opening and the subsequent ones at the colostomy problem. Shortly after the first colostomy was established, it prolapsed several inches. This was shortened surgically. Within a few months' time the colostomy then retracted. At operation, the descending colon was fixed to the parietal peritoneum. In August, 1949, a permanent single-barreled colostomy was done. In October, the single-barreled colostomy had stenosed, and this was corrected surgically. In December, 1949, the colostomy again prolapsed and a plastic surgical procedure was done. After this the colostomy gave no further technical troubles.

Unsatisfactory attempts to correct an imperforate anus in a boy at birth were followed by progessive difficulty in defecation until, at the age of 9 years, fecal impaction reached the spenic flexure and colostomy became necessary. Subsequent examination of the remaining fistulous anal tract suggested that restoration of continence might still be possible. This was accomplished at the age of 12 by carefully planned plastic surgery in two stages. The second stage, in which the colostomy was closed, was carried out only after the patient had acquired and demonstrated satisfactory sphincteric control by carefully graduated, highly disciplined exercises, with use of a perineometer and water pressure. Observations seven years after the operation show that the patient is active in athletics and has made an excellent scholastic and social adjustment.

The fistulous anal tract meanwhile had persisted in incontinent foul-smelling discharge and soiling. From the human interest point of view it produced quite a family problem. The mother stated that the boy was totally immune to the odors not only from the fistulous drainage but from the colostomy soiling as well. Three teen-aged daughters in the family objected to the odors in their home when they brought in their friends. Beyond all this, the parents could well foresee the ostracism which would be in store for their son as he matured. The family history was negative for any developmental anomalies.

Diagnostic Survey.—Height, weight, and other body measurements and results of studies of the endocrine system were all within normal limits for a male of this age (fig. 1). On physical examination no other anomalies could be found. Results of laboratory studies of urine and blood were within normal limits. X-ray survey, including intravenous pyelograms, of heart, lungs, gallbladder, and gastrointestinal tract showed normal results except for x-rays of the colon. X-rays of the skull were normal. A scout film of the abdomen taken on June 21, 1951, showed a remnant of rectal pouch containing two large scybala, each measuring several centimeters in diameter. After this a catheter was inserted into the fistulous tract and barium introduced. At the same time a barium enema was done through the colostomy stoma. The film (fig. 2) shows the relationship of the rectal pouch and the colon. Except for considerable shortening of the descending colon, the colon appeared quite normal.

This boy had a higher than average I.Q. He did very well in school. He had no discernible conflicts.

Analysis.—After a great deal of thought and study had been applied to this boy's problem it did not appear to be hopeless. The number one problem was whether or not a workable, functioning sphincter ani muscle could be constructed and developed. He had the rectal pouch and the

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anal fistulous tract, totally divorced from the single-barreled permanent colostomy. This was fortunate in that it provided an isolated unit of the problem for attack, which would in no manner disturb his health or digestive tract otherwise, while the plan for construction and development of the anal sphincter would be in progress. If a fully functioning sphincter could be provided, then transplanting of the colon to the rectal pouch would be justified. If the sphincter could not be made to perform fully, then the patient would be spared any further ordeal with his colostomy or any further abdominal surgery.

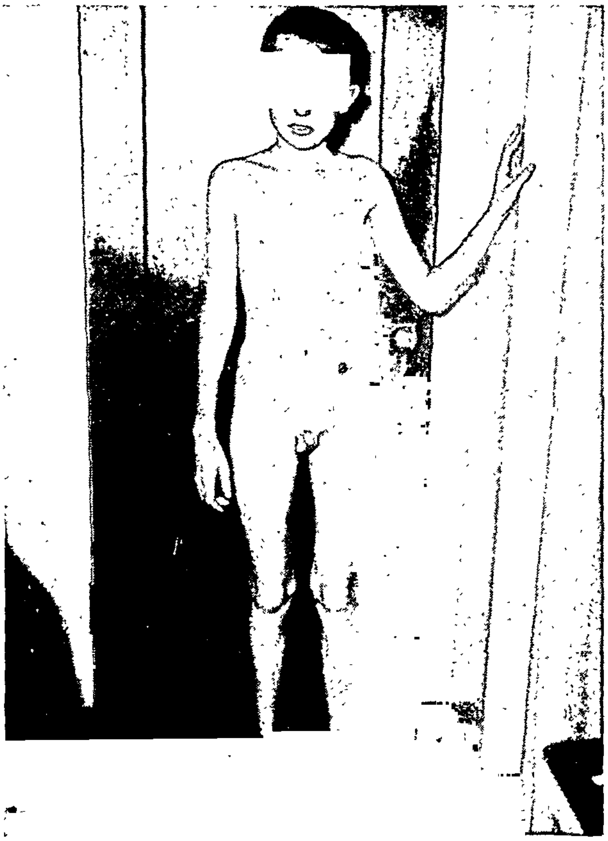

Fig. 1.—Twelve-year-old boy with permanent colostomy and anorectal fistula.

The Plan.—The projected plan was essentially simple. The first procedure would be a plastic reconstruction of the area of the anal plate. When healing had occurred, this would be followed by a regimen of carefully graduated exercises, scheduled, highly disciplined, and over a period of weeks or months. If successful, the results would not be elusive. A sphincter either works or does not work satisfactorily. If a satisfactory sphincter could be developed, then the colon would be brought down and joined with the rectal pouch and the colostomy removed.

While the plan appears simple, there are some basic factors to be considered. Each has an important bearing. Embryologically the internal and external anal sphincters are distinct entities, the external having a myoneural mechanism almost totally voluntary in control. Aside from subsequent aid from the accessory muscles of defecation, the external sphincter would be what we would have to work with. But this boy had never known a sphincter reflex, since he had always been incontinent and at 9 years of age had had the colostomy. The myoneural units of the external sphincter were surely present, even though totally undeveloped. This is readily demonstrable. As an example of undeveloped voluntary muscle, consider the three external ear muscles for moving our ears: Few people can move their ears because these muscles have not been developed. That they can be developed for entertainment purposes is readily recognized. It requires diligent exercise.

The next factor lay in the extensive scar tissue enveloping the anal sinus around which would be distributed the myoneural units of the external sphincter. This scar tissue had been built up over the 11 years from repeated attempts at repair and dilatations and the localized infections that naturally followed. By careful and diligent dissection followed by well-founded plastic surgical principles, there was the possibility of salvaging enough of the myoneural units to reconstruct the sphincter.

Assuming success to this point we come to the commonest problem of imperforate anus, common indeed to any tubal tract, namely, scar tissue contracture and stenosis. This I was prepared to deal with from past partly related experiences.[3] If the new anal opening was packed in wide dilatation, with use of a vented pack and not less than 4 cm. in diameter, the new scar tissue would be laid down in this radius within the first 24 hours. Now, if the pack were to be left in for four or five days it would fall out of its own accord, leaving a widely dilated anal opening. After healing was satisfactory, the muscle exercises, if successful, would bring the opening down to zero, since the muscle pattern is such as to close the opening; and the scar tissue, having been cast in wide dilatation, would have to follow, not lead. A technical point here is that no raw surface be permitted in the anal opening to give rise to pain and later scar tissue. With absolute hemostasis and administration of antibiotics a primary healing could be anticipated.

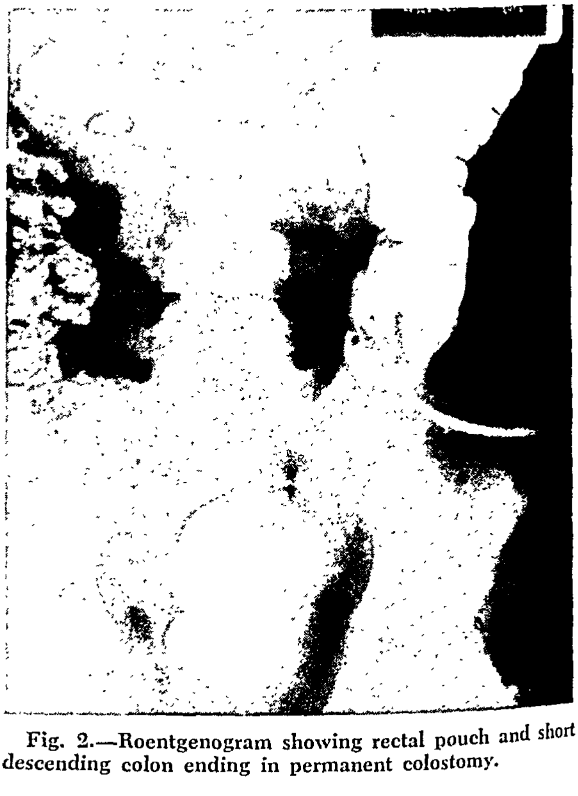

Fig. 2.—Roentgenogram showing rectal pouch and short descending colon ending in permanent colostomy.

If the surgical aspect of the sphincter problem went well, the next step would be the regimen of exercises, planned and graduated over a period of months if necessary. For the voluntary exercises of a muscle a counterpressure is necessary. For this purpose I planned to use the Kegel perineometer, for a number of reasons. The new anal orifice would be large to start with, and the compression cylinder of the perineometer is also large, having been designed for vaginal purposes. Additionally, the perineometer has a gauge which would indicate progress from day to day. If the patient succeeded with the perineometer, the next step would be a colon tube with graduated water pressure being increased as the boy made progress. If the progress with the colon tube were satisfactory, then the same routine with a catheter would be followed. Finally, if the plan were to be effective, the patient would have to be able to hold fluid in the rectal pouch for prolonged periods of time while he went about his daily routine at home and at school. If this last accomplishment could be obtained to the absolute satisfaction of the boy, his parents, and the surgeon, then the restoration of the bowel continuity would be warranted.

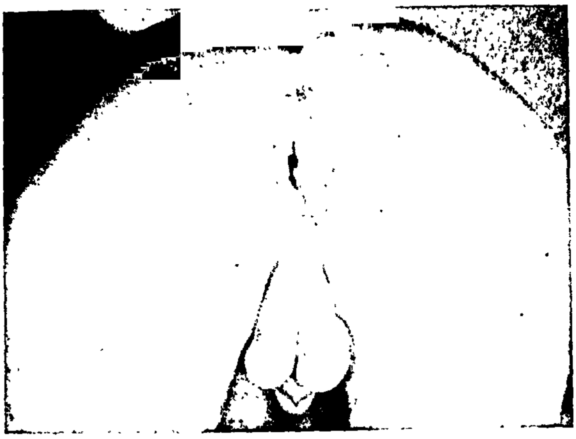

Fig. 3.—New anal opening healed in wide dilatation, before exercise regimen was begun.

This discussion and plan was presented to the boy and his parents. The parents readily accepted it. The boy wanted none of it since it meant at least one more operation and, if successful, still another operation. But he agreed to it. On July 23, 1951, I did the plastic reconstruction of the anal opening.

Surgical Procedure.—Under intratracheal anesthesia, the patient was placed in reverse Trendelenburg position on the table with the buttocks widely retracted by adhesive bands secured to the table. Beginning with the lubricated little finger, slow steady pressure was applied until the finger was fully beyond the stricture. Next the same procedure was carried out with use of the index finger and then the thumb; then the index finger of one hand and the little finger of the other hand were applied simultaneously until it was possible to insert a speculum into the opening. When the retractor was in place, the next procedure was directed at removal of the two large scybala which were known to be in the rectal pouch. It was possible to grasp the first fecal mass with a placenta forceps which served to steady the scybalum for further manipulation within the rectal pouch, since it was much too large to deliver through the opening. Thus steadied, the mass, which was very tough in consistency, was gradually divided and removed by morcellation. The same procedure was applied for the removal of the second large fecal mass, after which the rectal pouch was irrigated with sterile saline solution.

At this time careful examination of the nature of the stricture demonstrated that the anorectal mucosa came up to the inner border of the stricture in a reasonably sharp margin radially and had withstood the dilatation of the stricture without being torn. There was an extremely dense transverse scar tissue band on the border of the anus anteriorly. This appeared to present the greatest mechanical factor involved in the stricture. At this point I divided this band in the middle by an incision transverse to the band but in the longitudinal body axis. It then became apparent that dilatation was readily accomplished. This incision was extended inwardly down on to the normal mucosa and outwardly down to normal skin. With a slow tedious sharp dissection, with use of small instruments, the scar tissue was now dissected back from the center to normal skin externally. Most of the scar tissue appeared to be in the skin itself without too much invasion of the subcutaneous tissues. Dissection was carried inward to the mucosa where the scarring was minimal. In only a few points was it necessary to elevate the mucosa in order to eradicate the scar tissue.

The dissection having been completed, the anal opening was widely open. In order to gain the maximum mechanical advantage in the size of the opening, I now sutured the wound transversely to its original axis, using interrupted 000 chromic catgut suture on intestinal needles. The mucosa was likewise sutured to the skin margin with interrupted 000 atraumatic catgut suture, in those places where it had been elevated. This having been completed, it was possible to admit three fingers into the new anal opening. There were no denuded areas, and there was mucosa to skin apposition at all points. After this a large-gauge gum rubber tube was tightly wrapped with 4-in. gauze and impregnated with tetracaine (Pontocaine) hydrochloride ointment, until the diameter of the pack was approximately 4 cm. This was placed in the anorectal opening without any difficulty and secured firmly with dressings and tape. The patient lost very little blood during the operation. Postoperatively he received antibiotics. The pack came away on the fifth postoperative day. Healing was primary. Figure 3 shows the anal opening, widely dilated, after healing.

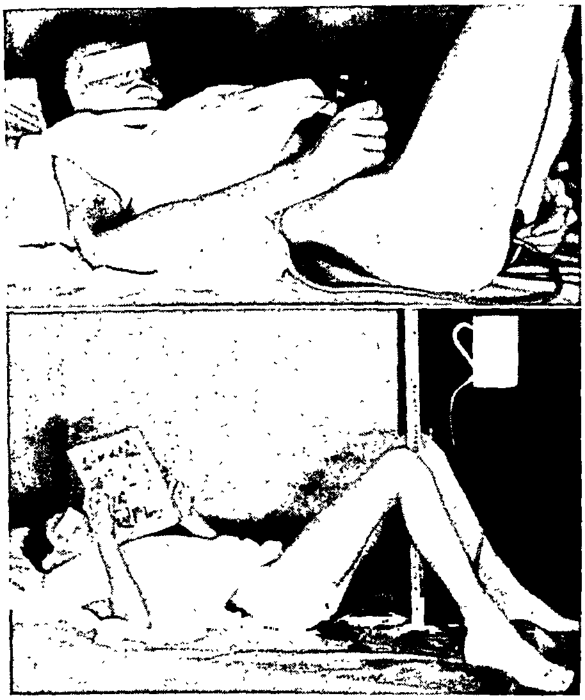

Fig. 4.—*Above,* first series of exercises begun with perineometer. *Below,* hydraulic phase of exercises with use of colon tube and enema can for pressure.

On July 31, 1951, the boy and his mother were instructed on the use of the perineometer in conjunction with a demonstration (fig. 4, *above*). It was necessary to impress on the boy that this was his project, that he would have to keep a daily log of all dates, readings attained, and time spent in exercises, and that he would have to bring this record to the office each time for inspection. This was necessary since he was prone to delegate all problems to his mother. The exercises with the perineometer consisted of 15 minutes of voluntary contractions on the pneumatic cylinder, performed three times each day while lying supine, and recording each time the height to which the gauge rose. His log records were extremely meticulous and neat.

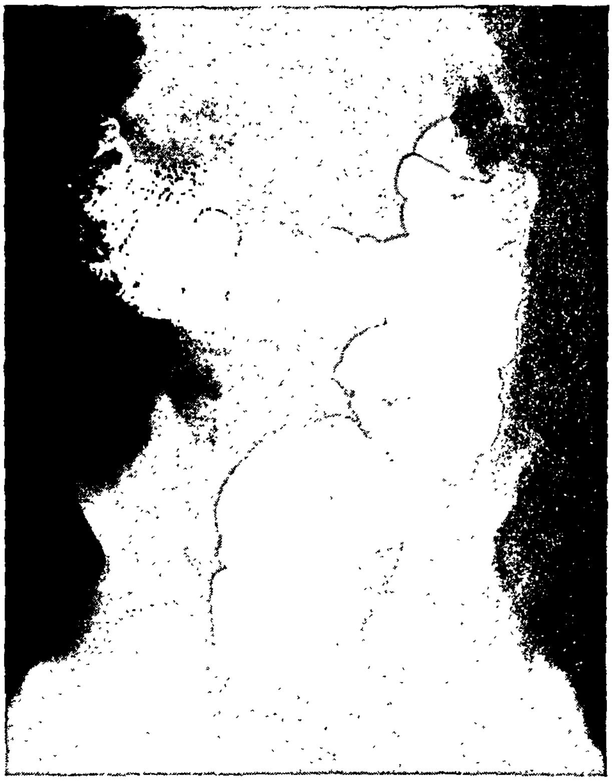

Fig. 5.—Roentgenogram of colon 10 months after restoration of intestinal continuity.

By Aug. 31, 31 days after the start of the exercises, his progress was so successful that he had exceeded the capacity of the perineometer. A satisfactory sphincteric contraction could be felt over the index finger. At this time the plan advanced to the hydraulic phase as scheduled. A colon tube was inserted into the anal opening, an enema can attached, and a yardstick used for a gauge (fig. 4, *below*). Again the program was for three 15-minute periods of exercise per day, being carried out in the bathtub at the start. By arrangement he was permitted to raise the can 2 in. if he had been successful in holding it without leakage in the previous exercise period. He was to continue his log. By Oct. 17, 1951, he had exceeded the yardstick elevation by an estimated 2 ft., for pressure. His sphincter contraction on the index finger was good. The colon tube was replaced with a catheter and the same exercise-pressure program carried out.

By Nov. 13, 1951, he could fill the rectal pouch under pressure, remove the catheter, play football for two hours, have no soiling, and then electively go to the toilet and expel it. The anal opening readily admitted the index finger without pain. He had positive satisfactory sphincteric control, in my opinion. I advised the parents that I was prepared to proceed with the abdominal phase of the plan but would prefer that they first have the boy checked by another surgeon of their choice in order to evaluate any enthusiasm which might seem warranted. This was immediately done by an officer of the U. S. Maritime Hospital. He concurred in the satisfactory status of the anal sphincter.

On Dec. 8, 1951, I did the abdominal phase of the plan. A detailed outline of the proposed surgery had been prepared for all assistants and nurses. Plan A called for the simplest procedure one could hope for, that is, mobilization of the descending colon and anastomosis of it to the rectal pouch. In view of the previous shortening and ventral fixation of the intestinal segment, plan A might not be workable. Under plan B I proposed to mobilize the splenic flexure in order to gain adequate length. Ordinarily this would not have appeared too formidable, but in view of the many previous operations and the shortening and ventral fixation, this plan might also not be feasible. Under plan C an alternative appeared, which had been noted in an upright film of the colon. This is not apparent in figure 2 because it is a prone film. The patient had an extensive ptosis of the transverse colon, and under plan C, if necessary, I planned to bring down the distal end of the transverse colon for the anastomosis.

After the abdomen was opened and the conditions estimated, they were found to be better than expected. It was possible to mobilize enough descending colon from above and enough rectal pouch from below to do an end-to-pouch anastomosis without any tension. The colostomy was removed. An appendectomy was done.

Postoperative convalescence was uneventful. On the third postoperative day the patient went to the toilet and had a bowel movement—fully controlled. He surprised us with his lack of enthusiasm over this event. On the morning of the fourth postoperative day he was in a state of great elation. He had been to the toilet and had sat for 30 minutes before allowing his bowels to move. His explanation for this happiness on this morning was that "It was the first time that I thought it would work." He left the hospital on the eighth postoperative day.

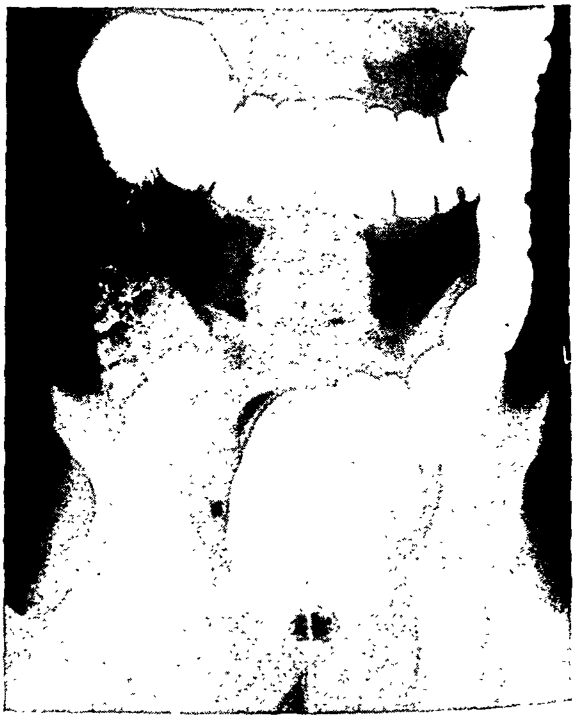

Fig. 6.—Roentgenogram of colon six and one-half years after restoration of intestinal continuity.

Results.—The patient returned to school after the Christmas holidays without loss of time. Contrary to plan he indulged himself in all of the varieties of the hamburger and

Coke diet, but without ill-effects. He has participated in athletics through high school and three years of college. *He has never had any dietary restrictions. He has never had* any dilatations of the anal opening nor need for them. His bowels move normally without any laxatives. He controls gas successfully. He can carry out the 2 oz. of castor oil regimen and drive 25 miles for a barium enema study. The first postoperative barium enema was done Oct. 11, 1952 (fig. 5). The last and only other study was done June 30, 1958 (fig. 6). The anal opening readily admits the index finger without pain. A fully satisfactory sphincteric contraction over the finger is readily demonstrated. The patient is now 6 ft. 5½ in. (197 cm.) tall and very successful in his third year of college.

Summary

A planned procedure for the problem, fortunately not common, of a young person with a colostomy and anal incontinence was carried out. It represented the combined application of sound plastic surgical principles, rehabilitation procedure for the development of the latent sphincter ani muscle, and restoration of bowel continuity and abolition of the colostomy. The theory advanced for the reconstruction of the anal sphincter in wide dilatation to avoid contractures, together with the subsequent muscle development program, may be a new approach. That it has been fully successful is encouraging. The principles can be applied in other procedures. It will be noted that this report has been delayed for seven years. This has been so elected in order that the boy reach maturity, that enough time elapse to permit proper evaluation of the results without undue enthusiasm.

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BLEEDING TENDENCY IN UREMIA

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Clues as to the reason for hemorrhagic phenomena among uremic patients were sought in a study of 65 men whose blood urea nitrogen levels were either above 24 mg. per 100 ml. or fluctuating about uremic levels. In 49 of the patients the blood urea nitrogen level was over 50 mg. per 100 ml. A series of tests was done, including the clotting time in glass, clotting time in silicone-treated glassware, one-stage prothrombin time, prothrombin consumption, platelet count, and, in some cases, thromboplastin generation, clot retraction, and capillary fragility. No impairment of clot retraction could be demonstrated in any of the patients, and no single test gave consistently abnormal results in these patients. There was, however, a rough correlation in that more of the tests gave abnormal results at the higher levels of uremia.

That uremia is associated with bleeding has been known since the turn of the century.[1] Mason[2] has reported that bleeding from the mucous membranes of the gastrointestinal tract occurs in 21.1% of the cases. Despite this knowledge, however, the mechanism of such bleeding is not known. Recently there have appeared in the literature several articles[3] which deal with this aspect of this perplexing problem. These articles have been inconclusive in their results. In few of them have serial determinations been done on a series of patients.

Since patients in a Veterans Administration hospital tend to be rehospitalized in the same hospital, it was decided to check the coagulation mechanism on any patient with a blood urea nitrogen level of more than 30 mg. per 100 ml., expecting that in this way more than one determination would be done on an individual patient as the uremic process progressed. By this method of selection, single coagulograms[4] were done on 42 patients with blood urea nitrogen levels ranging from 24 to

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186 mg. per 100 ml. and multiple coagulograms were done on 23 patients whose blood urea nitrogen levels were changing. This change was usually a progressive increase of the blood urea nitrogen level, although in some patients the level fluctuated and in others it showed a decline. The diseases represented in the multiple determinations are given in table 1.

Methods

A series of tests (coagulogram)[4] was done, consisting of clotting time in glass, clotting time in glassware treated with an organosilicate compound (Desicote), one-stage prothrombin time, prothrombin consumption, and platelet count. In selected cases, thromboplastin generation and capillary fragility tests were done.

The clotting time was done in three 75-by-8-mm. glass tubes at room temperature, the time of clotting in the third tube being taken as the clotting time. The same method was used in determining the clotting time in siliconized, treated glassware. Times up to 15 minutes were considered normal in glass, and times up to 55 minutes were considered normal in siliconized glassware.

TABLE 1.—*Disease Entities in Patients Given Multiple Coagulograms*

Disease	No. of Patients	No. with Clinical Bleeding
Arteriolar nephrosclerosis	6	2
Chronic pyelonephritis	3	0
Chronic glomerulonephritis	3	2
Chronic renal disease and cirrhosis of liver	2	1
Hydronephrosis and pyelonephritis	1	0
Adenocarcinoma of pancreas with acute pancreatitis and lower nephron nephrosis	1	0
Intercapillary glomerulosclerosis (Wilson-Kimmelstiel syndrome)	1	1
Diffuse hemorrhagic pericarditis of unknown etiology	1	1
Hemorrhage, shock, and oliguria after prostatectomy	2	2*
Nephrosclerosis and cortical necrosis	1	0

*Fibrinolysin found not to be a factor.

Prothrombin consumption was determined according to the method of Sussman and associates.[5] Commercially prepared fibrinogen was used. A time of less than 25 seconds was considered abnormal.

The one-stage prothrombin time was determined according to the method of Quick,[6] with use of thromboplastin prepared from human brain during the early part of the study and, later, commercially prepared rabbit brain. A control was recorded with each determination and the patient's value checked against it. The thromboplastin was prepared to give a normal value in the 14-to-15-second range.

The platelet count was done with a counting chamber, with use of both sides of the chamber and a calibrated red blood cell pipet. The diluting fluid used was a 1% solution of edathamil disodium (Sequestrene), colored with a few crystals of cresyl blue. Normal values were between 200,000 and 400,000 per cubic millimeter. The specimens were collected from siliconized glassware, and the value obtained by the direct count was checked against a coverslip preparation made from the same specimen and stained with Wright's stain.

The prothrombin consumption index was obtained by dividing the observed one-stage prothrombin time by the observed prothrombin consumption time. Since the same batch of thromboplastin was used in both determinations, variations due to the thromboplastin should be equalized. The normal range obtained on patients without known coagulation defects or bleeding tendencies was found to be 30-55%. This index was based on a formula devised by Merskey.[7] Abnormal consumption is denoted by values greater than 55%.

The thromboplastin generation test was done according to the method of Biggs and Douglas,[8] as modified by Bell and Alton.[9] Clot retraction was done according to the method of Budtz-Olsen.[10] No impairment in clot retraction could be demonstrated in any of the patients. These results are not quoted below. In no instance was any evidence of dissolution of the clot observed.

One hundred two coagulograms were done on 65 patients, 23 of whom had more than one coagulogram done during the course of illness. Of this latter group, 17 died. The thromboplastin generation test was done on 19 occasions on 15 patients, and results were always within normal limits, as judged by a concomitant examination on a normal control subject. Forty-nine of the coagulograms were done on patients having a blood urea nitrogen level of more than 50 mg. per 100 ml.

Results

The incidence of abnormalities occurring at the different ranges of blood urea nitrogen level is summarized in table 2. Table 3 shows the changes in the various tests of the coagulogram in relation to the change in the blood urea nitrogen level in the 23 patients who had more than one coagulogram. In addition to the patients included in these tables, two patients were studied who showed increasing abnormalities as the blood urea nitrogen level increased and then returned to normal as it decreased.

Since no constant defect in the coagulogram was demonstrated as the blood urea nitrogen level increased, it was decided to analyze the results according to the number of coagulation defects found at different ranges of the blood urea nitrogen level. The results are presented in table 4.

Comment

In table 2 are presented the results of the various tests in the coagulogram in all the patients with uremia included in this study. The percentages of abnormal results seem quite high in the lower levels of blood urea nitrogen, and this is particularly true of the prothrombin times. However, an analysis of the degree of abnormality reveals that of the 12 abnormal prothrombin times encountered in patients having a blood urea nitrogen level of more than 100 mg. per 100 ml., a group in whom it would be expected that such an abnormality would be significant, the range of difference between the patients and their controls was 1.4 to 8.5 seconds, with an average of 3.3 seconds. It is doubtful that such minor prolongation of the prothrombin time would be directly responsible for the clinical bleeding observed. Moreover, some of the patients studied had evidence of liver disease which was not related to or associated with the uremic process.

Table 2.—*Incidence of Abnormal Findings in Each Test of Coagulogram*

Range of Blood Urea Nitrogen Level, Mg. %	Coagulograms, No.	Abnormal Findings											
		One-Stage Prothrombin Time		Prothrombin Consumption		Clotting Time				Platelet Count		Prothrombin Consumption Index	
						Glass		Siliconized					
		No.	%	No	%	No.	%	No.	%	No.	%	No.	%
24- 50	40	19	47.5	3	7.5	0	0	1	2.5	8	20.0	12	30.0
51- 75	23	13	56.5	8	34.8	0	0	1	4.3	6	26.1	15	65.2
76-100	22	11	50.0	6	27.3	1	4.5	5	22.7	5	22.7	11	50.0
100+*	17	12	70.6	10	58.8	1	5.9	3	17.6	13	76.5	10	58.8
Total†	102	55	53.9	27	26.4	2	2.0	10	9.8	32	31.4	47	47.1

*Highest level, 186 mg. %.
†Totals show which tests were most frequently abnormal in patients with uremia.

From tables 2 and 3 it appears that the coagulation measurements most affected by an increasing blood urea nitrogen level are the one-stage prothrombin time, the platelet count, the prothrombin consumption, and the prothrombin consumption index. These tables reveal that the coagulation impairment is directly related to the height of the blood urea nitrogen level.

It has been claimed that the bleeding tendency in uremia is due to increased fragility of the capillaries.[3d] During the course of this study, several tourniquet tests were done and in none of them was there a greater response than 15 to 20 petechiae per circle of 2.5-cm. diameter. In one patient no coagulation defect could be demonstrated at a time when his blood urea nitrogen level was 120 mg. per 100 ml. and again when it was 140 mg., although he was oozing blood from his mucous membranes on both occasions and the tourniquet test finding was only 2+.

Table 3.—*Changes in Individual Coagulograms in Twenty-three Patients with Uremia, as Correlated with Changes in Blood Urea Nitrogen Level*

	Progressive Abnormality		Progressive Improvement		Results Unchanged with Changing Level, No.
	Rising Level, No.	Declining Level, No.	Rising Level, No.	Declining Level, No.	
Prothrombin time	9	1	2	2	10
Prothrombin consumption	8	0	1	0	14
Platelet count	9	0	2	0	12
Prothrombin consumption index	14	2	2	3	2
Clotting time, glass	1	1	0	1	20
Clotting time, siliconized	5	0	1	0	17

Other investigators in the field have felt that the platelets are at fault.[11] Larrain and Adelson[3a] and Larrain and Langdell[3b] felt that an inhibitory substance might be present. In all these investigations the platelet levels have been found to be low in some of the patients, but in few of them have they been low enough to be felt responsible for the clinical evidence of bleeding. These same investigators[12] have also found that in some of their patients there is a shortening of the prothrombin consumption time,[12] prolongation of the clotting time in siliconized glassware,[13] and abnormal thromboplastin generation.[3e] Lewis and co-workers[3c] found reduced thromboplastic function of the platelets in 8 patients, reduced accelerator activity in 7, and both in 4 of 12 patients studied.

My results are much in accord with these investigations with one important exception, namely, that the thromboplastin generation results were all within normal limits. Of the 19 such examinations performed, 6 were found to be in patients with abnormal prothrombin consumption and prothrombin consumption index yet having platelet counts in excess of 150,000 per cubic millimeter. It is most unlikely that the prothrombin consumption shortening and the prothrombin consumption index increase can be assumed to be on a basis of low platelet counts in these persons. In the method used,[9] a brain extract is substituted for the patient's platelets. This extract does not have thromboplastic activity but is capable of normalizing the thrombo-

Table 4.—*Total Incidence of Abnormal Coagulograms, Correlated with Blood Urea Nitrogen Levels*

Range of Blood Urea Nitrogen Level, Mg. %	Total No. of Tests	Abnormal Results	
		No.	%
24- 50	240	43	17.9
51- 75	138	39	28.3
76-100	132	39	29.5
100+	102	49	48.9

plastin generation test in platelet-deficient plasma. Therefore, this finding would seem to indicate that the platelets not only are quantitatively abnormal in some instances of bleeding but also may be qualitatively abnormal, as suggested by Rath and associates.[3e]

Whatever the underlying mechanism is, it is evident that, as the uremic process progresses, the number of coagulation abnormalities increases. Whether this is due to a deterioration of one of the factors which results in defects in the others measured, or whether the bleeding tendency is due to multiple coagulation deficiencies occurring separately as a result of the generalized deterioration of the patient, cannot be stated from this study. The normal clotting time (siliconized glassware) in most of these patients would make the possibility of a circulating anticoagulant unlikely. Also, the fact that the thromboplastin generation findings were normal would seem to argue against the presence of an inhibitor unless it had a specific effect on the platelets themselves. It does seem from the study that, if the bleeding is due to one factor, it is probably due to the defective formation of thromboplastin on a basis of a qualitative defect in the platelets.

Summary

A series of tests, including clotting time, one-stage prothrombin time, prothrombin consumption, platelet count, and, in selected cases, thromboplastin generation and the Rumpel-Leede test were done on 65 males whose blood urea nitrogen levels were elevated. Twenty-three of these patients had multiple tests as the blood urea nitrogen level was changing; most of them were tested as it was increasing. It was found that there was a rough correlation between the number of abnormal results and the height of the blood urea nitrogen level, with more of the tests giving abnormal results at the higher levels. While no single test finding tended to be consistently abnormal, the platelet count, the prothrombin consumption, and the prothrombin consumption index seemed to be most regularly affected. The bleeding tendency in uremia may be due to a qualitative defect in the platelets.

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Mrs. Myra Lowery supplied technical assistance in this study.

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INFECTION AND DIABETES.—Even a mild infection may considerably increase the severity of the diabetes and require much more insulin than is usually given. When the infection is severe, as in carbuncles, appendicitis with peritonitis, or empyema of the gallbladder, the diabetic patient may be easily pushed into acidosis or coma. Greatly increasing the amount of insulin may or may not control the acidosis or the coma, and in order to restore the patient to his pre-acidotic condition it may be necessary to operate upon him and rid him of the infection. In such an emergency, one would have to operate in the presence of uncontrolled diabetes and then try to control the acidosis in the postoperative period. Attention should also be called to the fact that, once the patient is free of the infection, his insulin requirements may rapidly diminish. The physician must be on guard for this probability in order to avoid producing insulin shock.—D. H. Wagner, M.D., The Preparation and Care of Diabetic Patients Requiring Surgery, *The Surgical Clinics of North America*, February, 1959.

SAFFLOWER OIL-PYRIDOXINE AND CORN OIL-PYRIDOXINE EMULSIONS

THEIR EFFECT ON SERUM CHOLESTEROL LEVELS IN YOUNG ADULT MALES WHEN USED AS SUPPLEMENTS TO A NORMAL DIET

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The effects of using safflower oil and corn oil as supplements to the usual diet were studied in 22 young healthy men. Serum was obtained weekly from each subject by venipuncture, to be analyzed for total cholesterol. Determinations during an initial observation period of five weeks afforded a basis for dividing the subjects into two matched groups with equal mean serum cholesterol levels (221 mg. per 100 cc.). One group thereupon received a supplement of safflower oil for seven weeks followed by corn oil for seven weeks; the other group received corn oil for seven weeks followed by safflower oil for seven weeks. In both groups a consistent decline in the mean cholesterol levels was observed as the experiment progressed, but the changes were not convincing because of the wide individual variations and no differences between safflower and corn oil were revealed under the conditions of this experiment. Significant cholesterol-lowering effect of these two oils can be demonstrated only if they are used as replacements for, rather than additions to, some of the saturated fats in the usual diet.

When unsaturated vegetable oils are substituted for saturated animal fat in the human diet, sustained reductions in levels of serum lipids can usually be achieved.[1] It was therefore to be hoped that vegetable oils could be used as supplements to the regular diet, so that reductions in levels of total serum cholesterol and other lipids might be possible without the restrictions of a low-fat diet. Several vegetable oil emulsions have been marketed recently and have been widely used in the treatment of patients with hypercholesteremia and arteriosclerosis.

Safflower oil and corn oil are the two oils most commonly used at present. Several of the emulsions of these oils now available also contain pyridoxine, which may be involved in fat metabolism.

An earlier report [2] from this laboratory described an experiment in which a safflower oil emulsion (without pyridoxine) was administered, with placebo controls, as supplements to young male volunteers who were maintained on an otherwise normal diet. Figure 1 is reproduced to show the results of that study, in which essentially the same group of volunteers participated as were used in the present study. No demonstrable depressant effect on total serum cholesterol levels was observed, although the volunteers took 50 Gm. of the oil daily for seven weeks.

The present experiment was designed to test the effects on the serum cholesterol level in 22 young male subjects of a safflower oil emulsion with pyridoxine and of a corn oil emulsion with pyridoxine, each used as a supplement to the usual diet.

Materials and Methods

Selection of Subjects.—Twenty-two young male medical students, averaging 24 years of age (range 22 to 26) were selected to serve as paid volunteers. All but one of these had served as volunteers in the previous experiment. None had a history or clinical evidence of atherosclerosis or thyroid disease.

Control of Diet.—Questionnaires were used to establish the following average composition of the diet: total calories, 2,400 (range 1,900 to 3,100); calories derived from fat, 40% (range 32 to 45%); and total daily fat intake, 102 Gm. (range 86 to 116 Gm.). The subjects were asked to adhere as closely as possible to their usual diets throughout the experiment but were allowed to omit desserts if they found themselves gaining weight. Each subject was weighed weekly.

Experimental Design and Method.—Serum was obtained weekly by venipuncture, with the subject in the fasting state, and analyzed for total serum cholesterol level by a modification of the method of Bloor. Most determinations were made with fresh serum, although some were performed with serum which had been frozen for several days at –15 C.

There was a preliminary control period of five weeks, during which time the subjects followed their usual activities and diets. At the end of this period, the 22 subjects were matched according to nearest average serum cholesterol levels observed

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that far in the experiment. Half of the volunteers were then given a safflower oil emulsion supplement and half a corn oil emulsion supplement. Because the two preparations available differed in their water content, 150 cc. daily of safflower oil and 90 cc. daily of corn oil were prescribed. However, these dosages both contained an equal amount by weight of the particular oil, approximately 45 Gm. daily.

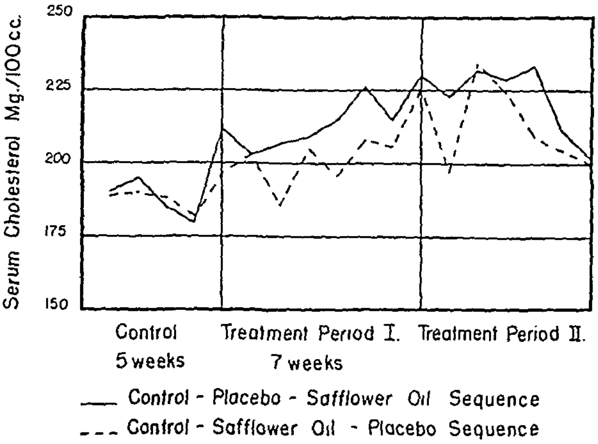

Fig. 1.—Mean total serum cholesterol levels in two groups of 12 subjects each.

The safflower oil emulsion contained linoleic acid (as safflower oil), mixed tocopherols, glycerine, emulsifying agents, polysorbate 60, sorbitan trioleate, artificial sweetener calcium cyclamate, artificial flavoring, 0.1% sodium benzoate, and 0.004% propyl gallate plus pyridoxine hydrochloride. The daily dose used contained 45 Gm. of safflower oil and 50 mg. of pyridoxine hydrochloride. The corn oil emulsion contained corn oil, polyoxyethylene sorbitan monostearate and fatty acid monostearate and fatty acid monoglyceride and diglyceride as emulsifiers, natural and artificial flavors, coloring material, 0.005% propyl gallate, and 0.1% sodium benzoate plus pyridoxine hydrochloride. The daily dose used contained 45 Gm. of corn oil and 20 mg. of pyridoxine hydrochloride.

Table 1.—*Weekly Serum Cholesterol Level Determinations, in Milligrams per 100 Cc., During Control, Safflower Oil, and Corn Oil Treatment Periods*

	Control						Safflower Oil								Corn Oil								
Case No. Week No.	1	2	3	4	5	Av.	6	7	8	9	10	11	12	Av.	13	14	15	16	17	18	19	Av.	20*
1	...	232	232	202	196	219	252	231	220	188	205	205	159	208	208	202	200	214	188	183	200	199	200
2	198	183	202	208	198	200	205	171	214	168	214	220	196	198	193	198	208	198	202	193	214	201	183
3	303	288	280	311	252	291	297	288	336	247	288	300	297	292	297	260	186	226	232	252	280	248	232
4	214	232	200	229	280	218	236	290	288	247	226	239	232	251	232	232	247	232	239	220	260	237	252
5	138	129	154	168	121	147	208	143	...	133	161	171	163	163	168	147	147	117	143	138	147	144	143
6	280	220	252	247	214	240	193	236	214	173	196	202	205	202	214	214	198	208	214	198	214	209	200
7	226	200	239	243	239	232	232	229	239	220	223	226	191	223	232	214	211	226	193	177	208	209	208
8	303	247	273	252	264	267	256	252	252	273	243	226	226	247	226	247	208	...	...	208	226	223	232
9	223	177	163	188	168	184	183	166	...	159	193	193	173	178	188	177	193	183	198	188	214	192	183
10	273	260	267	226	247	254	226	210	239	247	239	247	232	239	243	229	217	250	232	232	239	235	232
11	202	188	183	196	188	194	220	240	220	208	188	214	198	213	198	198	177	168	168	...	193	177	208
Over-all average	236	211	222	225	215	225	228	226	235	206	216	222	207	219	218	211	199	202	201	199	218	207	207

* Final determination after 1 wk. without any supplement.

After seven weeks of therapy, the two experimental groups were reversed, so that those who had taken safflower oil then took corn oil and those who had taken corn oil then took safflower oil. After a total of 14 weeks of therapy, use of the vegetable oil supplements was discontinued and one final cholesterol level determination was performed after each subject had been without any supplement for a week.

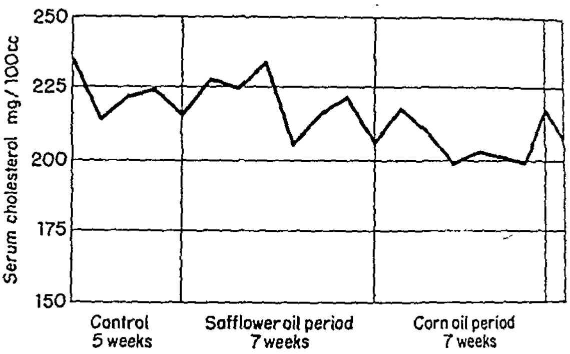

Fig. 2.—Mean total serum cholesterol levels in 11 subjects: control, safflower oil, corn oil treatment sequence.

Plasma studies in certain of the volunteers were done serially by means of the thrombelastograph, the results of which will be the subject of a separate report from this laboratory.[3]

Results

As had been the case in our previously reported study,[2] there was a considerable variation from week to week in the cholesterol levels of the individual subjects. The over-all average, however, during five weeks without therapy was 221 mg. per 100 cc. (range 125 to 311 mg.).

The addition of 150 cc. of safflower oil emulsion with pyridoxine (containing 45 Gm. of oil) to the daily diet of 11 of the subjects was followed by a slight decrease in the average serum cholesterol level (fig. 2). When, after seven weeks of this, 90 cc. of a corn oil-pyridoxine emulsion (again containing 45 Gm. daily of vegetable oil) was substituted, there continued to be a gradual downward trend in the average cholesterol level (table 1).

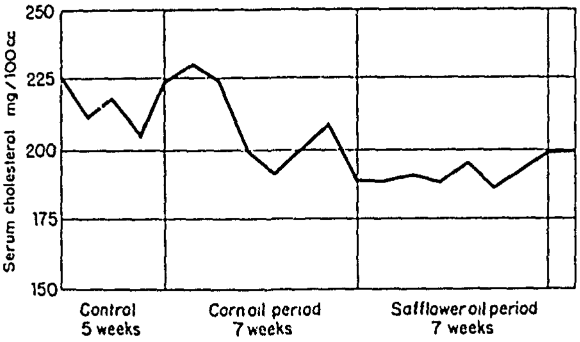

Fig. 3.—Mean total serum cholesterol levels in 11 subjects: control, corn oil, safflower oil treatment sequence.

In the other group of 11 subjects, with whom the sequence of therapy was reversed, similar results were obtained, i. e., a slight, gradual decrease in the average serum cholesterol level (fig. 3, table 2). In each group the corn oil-pyridoxine emulsion appeared to be slightly more effective.

However, the decrease in average serum cholesterol level during therapy was at no time statistically significant, whether any single week or the entire seven-week treatment period was taken as an example. That is, the decrease in average serum cholesterol level at no time was more than twice the standard deviation from the mean established during the control period.

Table 2.—*Weekly Serum Cholesterol Level Determinations, in Milligrams per 100 Cc., During Control, Corn Oil, and Safflower Oil Treatment Periods*

Case No.		Control						Corn Oil								Safflower Oil								
	Week No.	1	2	3	4	5	Av.	6	7	8	9	10	11	12	Av.	13	14	15	16	17	18	19	Av.	20*
1		173	183	220	180	232	195	239	229	188	193	183	200	193	204	188	168	168	183	161	173	183	175	177
2		260	239	208	200	260	233	250	220	209	208	239	252	211	227	193	202	200	193	214	193	208	203	208
3		303	288	250	220	273	265	234	202	231	214	214	273	232	229	...	239	229	...	267	252	267	251	247
4		208	183	202	202	202	197	173	175	...	193	202	193	183	187	191	183	177	198	183	202	188	188	163
5		273	264	280	202	243	252	243	198	208	220	...	232	198	217	211	220	217	214	193	239	214	215	198
6		270	247	311	260	252	268	339	252	...	239	223	252	247	244	183	208	226	232	166	193	208	202	252
7		285	186	226	208	226	226	226	223	198	186	198	220	168	203	214	208	191	214	208	208	214	208	...
8		157	163	133	198	191	173	188	172	173	147	161	168	121	161	157	145	150	168	168	138	193	160	168
9		220	247	236	226	208	224	267	240	239	198	214	...	183	224	220	208	220	239	202	198	183	210	226
10		129	125	138	138	125	131	136	125	145	109	141	125	138	131	125	117	116	114	105	102	129	115	154
11		200	208	188	208	247	212	...	231	193	...	220	177	191	198	200	191	177	188	183	214	193	192	193
Over-all average		226	212	218	204	224	217	230	224	198	191	200	209	188	202	188	190	188	194	186	192	198	193	199

* Final determination after 1 wk. without any supplement.

There was very little weight gain noted in these subjects. The average weight gain after 14 weeks' therapy with both vegetable oil emulsions was 0.6 kg. (1.3 lb.). In general, the oil emulsions were tolerated well, despite the large doses used. Occasional episodes of loose stools were reported.

Comment

Rivin and associates [1] have recently emphasized the fact that there may be a considerable biological fluctuation from time to time in total serum cholesterol levels of patients; they pointed out that caution is necessary in drawing inferences from a single cholesterol level determination. The results of the present study, in which wide fluctuations from week to week were observed in individual subjects' cholesterol levels (during both control and treatment periods) reinforce this view.

There is little doubt, however, from the reports of other experimenters, that the use of either corn oil or safflower oil, substituted for most of the fat in the diet, will produce a significant decrease in serum cholesterol levels. But, in this study, the results of the use of these oils as supplements to a regular diet were not significant enough to justify this as a therapeutic procedure.

Similar studies were made on a small group of patients with elevated serum cholesterol levels (more than 300 mg. per 100 cc.). These results will not be reported here in detail, but they resemble the results obtained in the young male volunteers. That is, no significant decrease in serum cholesterol level followed the use of vegetable oil supplements when the diet contained moderately high amounts of saturated fat. But, when a strict low-fat diet was used, the addition of corn oil or safflower oil supplements usually produced a greater decrease in the serum cholesterol level than had the low-fat diet alone.

The results of the experiment reported here support the idea that, when a lowered serum cholesterol level is desired, corn oil and safflower oil are best used as supplements to diets markedly reduced in their content of saturated fat. Significant results should not be expected from the use of corn oil or safflower oil, even with the addition of pyridoxine, as a supplement to the usual American diet. The slight downward trend noted in this study may have been related to the pyridoxine or other ingredients included in the emulsion, since it was not noted with safflower oil alone. Since the effect was, however, not significant statistically, this question is not clearly answered.

Summary

Twenty-two young male subjects were studied during a three-phase experiment lasting 19 weeks. After a five-week control period, they were given, in sequence for seven-week periods, a daily dietary supplement of an emulsion containing pyridoxine hydrochloride and 45 Gm. of either corn oil or safflower oil. The slight decrease observed in average serum cholesterol level was not found to be statistically significant.

This study reemphasizes the fact that, if one wishes to produce a significant lowering of the serum cholesterol level, unsaturated fats should be used only when combined with a diet which sharply limits the use of saturated fats.

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The safflower oil emulsion used in this study was supplied as Linodoxine by Pfizer Laboratories Division, Chas. Pfizer & Co., Inc., New York. The corn oil emulsion was supplied as Atheroxin by Gray Pharmaceutical Co., Newton, Mass.

Mrs. Lorraine Rose and Miss Ann Florio provided technical assistance in this study.

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SUBLUXATION OF THE HEAD OF THE RADIUS IN YOUNG CHILDREN

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Subluxation of the radius at the elbow in children results easily from a combination of pulling and twisting forces. In the seven cases here described the most frequent age was 3 years; the youngest and oldest patients were 10 months and 4 years of age. Three fell while at play, two fell while being held by the arm, one was lifted by the arm, and one had his arm twisted by a playmate. Reduction of the dislocation required but little force and sometimes occurred spontaneously or during examination. The technique for reduction here described involves supination of the forearm while the elbow is held in the extended position and slight pressure is applied to the head of the radius by the physician's thumb. The success of the maneuver is usually attended by a slight clicking sound and immediate relief of pain.

A frequently occurring condition which responds to simple treatment is subluxation of the head of the radius in young children. The injury usually occurs between the ages of 2 and 4 years and is rare after the age of 6. The cause is forcible traction on the extended and pronated forearm and frequently is brought about when the child is lifted by the arm or stumbles while walking when held by the hand, throwing his weight on the arm. After injury there is pain in the region of the elbow, the child refuses to use the arm, and he holds the elbow slightly flexed and the forearm pronated.

The injury was described many years ago and has been known by a variety of names; among these are Malgaigne's luxation, luxation by elongation, nursemaid's elbow, and Gromeyer's injury. Griffin[1] credits Fournier[2] with the first accurate description in 1671. As described by Fournier, the injury caused incomplete dislocation of the head of the radius, relaxation of the ligaments, and downward separation or elongation of the bone. Treat-

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ment consisted of supination of the forearm with pressure on the head of the radius followed by flexion of the forearm at the elbow.

Van Arsdale,[3] in a paper read before the surgical section of the New York Academy of Medicine, noted that Hippocrates and Celsus "referred to the matter" and that histories of the subject were given by Malgaigne[4] and Streubel.[5] One hundred consecutive cases were presented in tabular form, giving the age and sex of the child and the nationality of the parents in each instance. He noted that the frequency of the condition was over 1% of surgical injuries in children. Most of his cases were in children 4 years of age or younger. One child was aged 8 years and 6 months. Reduction was accomplished by forced supination and followed by splinting to prevent recurrence.

Stone[6] in 1916 noted that Van Arsdale attributed the injury to the eccentric shape of the radial head, the epiphysis of which became pushed to one side, impinging on the ulna. In an attempt to determine the anatomic explanation of the subluxation, he carried out a number of experiments on 12 arms from material in the anatomic laboratory of the Washington University Medical School. The muscles were removed from these arms, but the ligaments were left intact. When forcible traction was applied to the first arm, the annular ligament could be seen to spring inward, but, on powerful adduction, the external lateral ligament ruptured. In the remaining 11 elbows, subluxation of the radial head was produced in 6. In each of these arms the annular ligament always slipped over the head when the hand was pronated. In the four arms the ligament tore when traction was applied with the hand supinated.

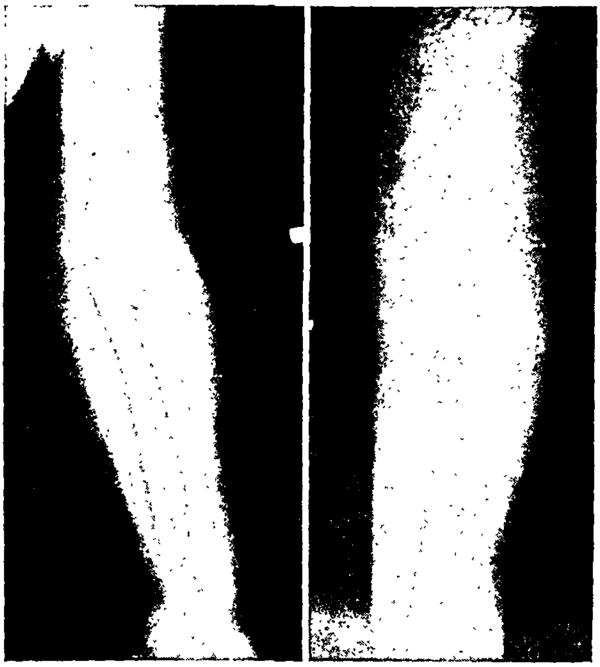
Stone also noted that, whereas standard textbooks on anatomy gave the shape of the radial head as round, measurements of 100 specimens revealed one diameter to be 1.5 mm. greater, on the average, than the other. In some bones the diameter difference was as great as 3 mm. The long diameter was always found to be in the same sagittal plane as the interior portion of the tuberosity of the radius. From these findings Stone explained the reason for subluxation occurring when the forearm was in pronation as follows: "Anteriorly, from the neck of the radius to the head, the rise is an abrupt one. Any traction with the hand supine pulls the ligament against this. Laterally and posteriorly the ascent is quite gradual, so that in pronation the ligament lies over this part and is stretched until it suddenly slips over the head."

Diagnosis

The injury occurs in a child usually between the ages of 2 and 4 years. A history of forcible traction on the extended and pronated forearm is usually described but not always obtained. After injury the child complains of pain in the region of the elbow and holds the elbow slightly flexed with the forearm pronated. The parent notes that the child refuses to use the arm and that attempts to supinate the forearm are painful. Palpation may reveal slight tenderness over the head of the radius, and occasionally the head of the radius may be somewhat more prominent than on the opposite side. Extension and flexion of the elbow are normal. Results of roentgenologic examination are usually negative, but occasionally slight separation between the head of the radius and the capitellum may be visible (see figure).

Treatment

Treatment of subluxation of the head of the radius in children is simple. The subluxation is easily reduced by manipulation as follows: The affected elbow is grasped with one hand with the thumb on the head of the radius. The forearm is held with the opposite hand at the wrist and extended. The forearm is then forcibly supinated, and at the same time slight pressure is made on the head and neck of the radius with the thumb. Upward pressure may be made on the forearm along the shaft of the radius compressing it against the capitellum of the humerus. As supination is carried out a slight click is often felt over the head of the radius, and pain and limitation of supination are relieved. Reduction is usually so easy that it may occur spontaneously or be accomplished by the parent or x-ray



Left, slight widening of joint space between proximal radius and capitellum of humerus, with elongation of radius at wrist. *Right,* normal forearm.

technician during manipulation of the arm. After reduction it is advisable to place the arm in a sling for a few days. The parents should be warned to avoid traction on the child's forearm for several weeks.

Report of Cases

CASE 1.—A 10-month-old child fell while being held by the right arm by his mother on Oct. 15, 1951. The child immediately began to cry and refused to use the arm. Examination revealed normal extension and flexion of the arm at the elbow. Supination of the forearm was limited, with pain on forcing. As supination was carried out, a mild click was palpated over the head of the radius and pain was relieved. An x-ray of the elbow was made and was normal. A long arm plaster splint holding the elbow at 90 degrees was applied and remained for four days.

CASE 2.—A 3-year-old boy was seen April 7, 1952, complaining of pain in the right wrist. Two days previously, while playing, his sister had rolled on his right arm. After the injury his parents noted that he refused to use the arm and complained of pain whenever the arm was touched. Examination revealed extension of the right forearm at the elbow to 175 degrees and flexion to 30 degrees. There was tenderness over the head of the radius. The child held the arm slightly flexed at the elbow with the forearm pronated. X-rays of the extremity were normal. A diagnosis of subluxation of the radial head was made. The dislocation was easily reduced by extension of the forearm at the elbow, followed by supination with pressure over the radial head.

CASE 3.—A 4-year-old boy, while playing with his 13-year-old cousin, complained of pain in the left elbow. The parents were unable to give a clear explanation of the mechanism of injury, but the child stated that the cousin twisted his arm. He was seen in the office July 28, 1952, the day after the injury. Examination disclosed tenderness over the head of the radius and pain and limitation of supination of the forearm. Extension and flexion of the elbow were normal. An x-ray of the elbow and forearm was normal. A diagnosis of subluxation of the head of the left radius was made. Reduction was carried out by extension of the elbow, followed by supination of the forearm with pressure over the radial head.

CASE 4.—A 2-year-old girl was seen May 27, 1953, because of pain in the left arm and elbow. The mother stated that one week previously, while she was walking downstairs holding the child by the left arm, the child fell, sustaining a pulling injury to the arm. Since the accident the child failed to use the arm normally and complained of soreness about the elbow. Examination revealed supination of the left forearm to be limited, with pain on forcing. Flexion and extension of the elbow were normal. An x-ray of the left upper extremity was made and was normal. A diagnosis of subluxation of the left radial head was made. The forearm was forcibly supinated with the elbow extended, with relief of pain. A posterior plaster splint was applied holding the elbow at 90 degrees flexion and was worn for one week. At the time the splint was removed full supination was present and the child had no pain in the extremity.

CASE 5.—A 2-year-old boy was lifted by his left arm on June 5, 1954. The child immediately began to cry and refused to use the extremity. Examination revealed the child to hold the left forearm in pronation. Attempts to move the wrist or elbow were resisted. X-rays were made of both upper extremities and were normal. Forced supination of the forearm resulted in an audible click, and pain was immediately relieved. A plaster splint was applied to the extremity, holding the elbow at 90 degrees. A week later the cast was removed and the child moved the extremity normally and without pain.

CASE 6.—A 3-year-old girl was seen in the office July 26, 1958. The day previous, while playing with a water hose in the yard, she had fallen and injured the left arm. After the injury she complained of pain about the elbow and refused to use the arm. Examination revealed that the child held the left forearm pronated with the elbow slightly flexed. There was tenderness over the head of the radius, and supination of the forearm was limited, with pain on forcing. The child was sent to the x-ray department for an x-ray of the elbow, and as the forearm was extended during exposure of the films a slight snap occurred in the region of the head of the radius and pain disappeared. The x-rays of the elbow were normal. A diagnosis of reduced subluxation of the left radial head was made.

CASE 7.—A 3-year-old girl was seen Aug. 5, 1958. The mother stated that while playing the child fell, injuring the left arm at the elbow. Examination revealed the left elbow to be held slightly flexed and the forearm pronated. There was no definite tenderness about the elbow, forearm, or wrist. An x-ray was made of the left upper extremity and revealed slight widening of the joint space between the head of the radius and the capitellum of the humerus. A diagnosis of subluxation of the radial head was made. The forearm was extended at the elbow and forcibly supinated, producing a click at the radial head with relief of pain.

Summary

Subluxation of the head of the radius is a traumatic injury occurring in children usually between the ages of 2 and 4 years. The injury is produced by traction on the pronated and extended forearm and causes symptoms of pain in the region of the elbow and limitation of supination of the forearm. X-ray examination may show negative results, but occasionally slight widening of the space between the head of the radius and the capitellum of the humerus is present. Reduction is accomplished by supination of the forearm with the elbow extended, accompanied by slight pressure over the head of the radius and compression of the shaft of the radius against the capitellum of the humerus. A slight click may be palpated as reduction occurs. After reduction the arm should be supported by a sling for several days and traction on the forearm should be avoided for several weeks.

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SPONTANEOUS DISAPPEARANCE OF BILATERAL PULMONARY METASTASES

REPORT OF A CASE OF ADENOCARCINOMA OF KIDNEY AFTER NEPHRECTOMY

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A 65-year-old man, hospitalized because of general weakness and striking weight-loss, was found by roentgenography to have pulmonary lesions suggesting metastases of a tumor. Intravenous pyelography gave evidence of a malignant tumor of the left kidney. A nephrectomy was performed, and the lesion proved to be a clear-cell serous papillary cystic adenocarcinoma. The condition of the patient remained poor for about three months, and the pulmonary lesions increased in size and number. The patient then improved, and at the time of discharge from the hospital the pulmonary lesions were no longer visible. Similar observations have been made in the past. They suggest the hypothesis that these tumors have distinctive properties as to origin and biological activity.

There are only a few cases reported in the literature of spontaneous disappearance of pulmonary metastases of an adenocarcinoma of the kidney. Mann[1] described three cases in which the metastases were present before nephrectomy and disappeared after the primary tumor was removed. One similar case was reported recently by Arcomano and co-workers[2] in which the metastases present before nephrectomy disappeared eight months after operation. There are two more cases, one reported by Bumpus,[3] the other by Beer,[4] in which the metastases appeared after nephrectomy and disappeared spontaneously about five months later.

The number of these cases is rather low if we take into consideration the facts that kidney tumors constitute about 2% of all malignant tumors in adults and that about 80% of all malignant renal tumors are adenocarcinomas.[5] The reason for this may be the prevailing opinion that nephrectomy in the presence of metastases is a questionable procedure[6] and should be done only if the metastatic lesion is isolated and can be removed at the same time as the kidney. Campbell[7] expressed a similar opinion that nephrectomy is the preferred treatment for renal adenocarcinoma (hypernephroma) in the absence of metastases. Referring to the cases of Mann,[1] Bumpus,[3] and Beer[4] he also recommends nephrectomy when only a single metastasis is present, but without removal of the metastasis.

Report of a Case

A 65-year-old man was admitted with the chief complaints of general weakness and loss of 20 lb. (9.1 kg.) of weight in the four weeks before admission. He had been treated in this hospital in 1952 for a left-sided hemiparesis due to cerebral thrombosis, with complete recovery after six months of treatment. He had had no other diseases until the present admission.

Physical findings on admission were essentially unremarkable. The chest x-ray showed several bilateral nodular densities considered to be metastatic lesions. A series of x-ray studies of bone showed no further metastases. Laboratory findings were essentially within normal limits, except for a leukocyte count of 19,920 per cubic millimeter with a normal differential count, and 12 erythrocytes per high-power field in the urine sediment.

In search for a primary tumor intravenous pyelography was performed and the findings showed evidence of a malignant tumor of the left kidney. A nephrectomy was performed and a clear-cell serous papillary cystic tumor (papillary adenocarcinoma) was found. The patient's general condition remained poor for three months postoperatively. A roentgenogram of the chest made two months after surgery showed the metastatic nodules increased in size and number (fig. 1). During the next several weeks the patient started to improve slowly and a chest x-ray made three months after operation showed striking regression of the multiple nodular lesions. The patient continued to improve and gained 20 lb. in weight. A chest x-ray made four months after operation showed complete clearing of both lung fields. The patient was discharged and was followed up on an outpatient basis. The last roentgenogram of the chest, made seven months after operation, showed both lung fields to remain clear (fig. 2).

Comment

Adenocarcinomas of the kidney are classified into three groups[6]: (1) serous papillary cystic tumor (papillary adenocarcinoma) with clear cells or with granular cells, (2) malignant cystadenoma, and (3) alveolar carcinoma. These tumors differ to some extent as to the degree of malignancy. The papillary adenocarcinoma with clear cells, previously called hypernephroma,[7] constitutes the most frequent type of renal tumor.[6] It is interesting that, in all reported cases in which the pulmonary metastasis disappeared after nephrectomy, the kidney tumor was a clear-cell adenocarcinoma. This could lead to the assumption that these tumors may be different in origin and biological activity from other adenocarcinomas of the kidney, as they are less malignant, grow slowly, and often become very large before causing any symptoms.

It is known that metastasis of choriocarcinoma (chorioepithelioma) to the lung may also disappear after removal of the primary tumor.[8] Peterson[8a] first suggested that this may be due to specific antibodies (syncytiolysins), which are produced when chorionic cells reach the maternal blood

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From the State Veterans Hospital.

stream during pregnancy or labor. Bumpus,[3] referring to Peterson's theory of lysins, suggested that the same theory could also be applied to the cases of hypernephromas in which the pulmonary metastases disappeared spontaneously.

It can be assumed that during operation some microscopic parts of the tumor reach the blood stream and cause the production of antibodies (lysins). Some of the particles may develop into metastases before the titer of the antibodies has reached a level sufficient to dissolve them; they are, however, dissolved later, when the titer has increased to a high enough level. This would explain the cases reported by Bumpus[3] and Beer[4] in which the metastases appeared after nephrectomy and disappeared about five months later.

Sometimes the metastases do not appear at all after operation in spite of extension of tumor tissue into the renal veins (eight cases mentioned by Bumpus[3]). In these cases the titer of the antibodies probably increased so fast that the small particles which reached the blood stream during surgery were dissolved before they could grow. It is even more probable that small amounts of antibodies were present in blood before operation, as small tumor particles may break into the blood stream under normal conditions. The titer of these antibodies would be low before nephrectomy because of reaction to the primary tumor; but after nephrectomy, the titer would be high enough to dissolve the particles reaching the blood stream during operation and thus prevent metastases.

It was also observed that the general condition of almost all patients in the described cases was poor for several months after nephrectomy. This could be due to increased amounts of toxic products from the destroyed tumor cells. The morbidity of the patients before nephrectomy could also be due to these toxic products rather than to toxins produced by the tumor cells as is generally supposed.

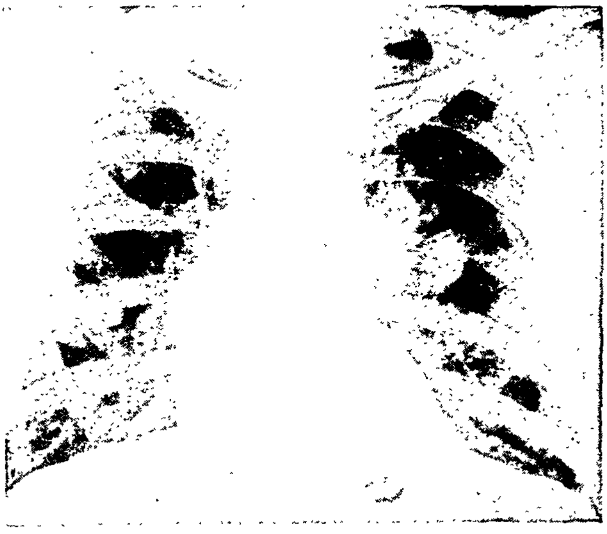

Fig. 1.—Roentgenogram of the chest made two months postoperatively, showing enlarged metastatic nodules.

The case presented by Arcomano and co-workers[2] is interesting because the patient developed a metastasis to the brain one year after the disappearance of the pulmonary metastases. This single metastasis was removed and the patient remained asymptomatic for 17 months after surgery. If we accept the hypothesis that antibodies are responsible for the disappearance of the pulmonary metastases, then the development of a metastasis to the brain would suggest that the antibodies either cannot pass the blood-brain barrier or are present there in much smaller concentrations than in the blood and, therefore, cannot prevent the growth of the metastatic cells.

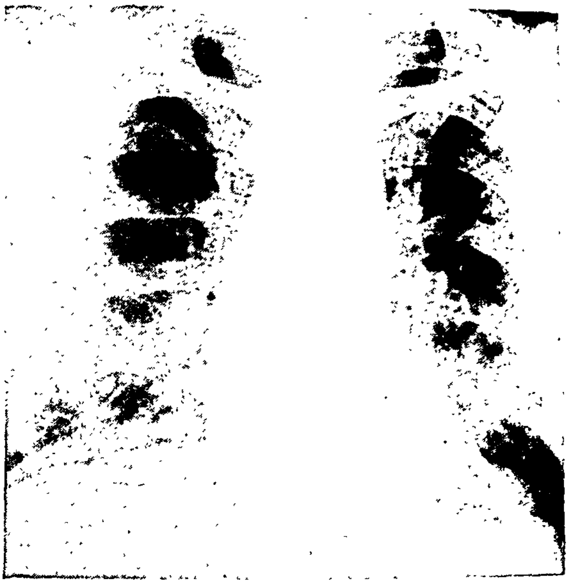

Fig. 2.—Roentgenogram of the chest made seven months postoperatively, showing clear lung fields.

The antibody theory of Peterson[8a] and Bumpus[3] could also explain why in some cases the metastases appear only after many years. An antibody titer which is not high enough to dissolve metastatic cells would still prevent their growth for many years rather than destroy them completely. If for some reason the antibodies disappear from the blood, then these cells are able to develop again and produce metastases.

All these considerations are of hypothetical nature, as in the last 30 years only these few cases have been described in the literature, and further investigations are needed to explain these interesting findings.

State Veterans Hospital, West Street.

Dr. Miriam Liberson, Chief of the Radiology Department, interpreted the roentgenograms.

Dr. Charles E. Jacobson Jr. performed the nephrectomy.

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DOUBLE-BLIND EVALUATION OF METHYLPHENIDATE (RITALIN) HYDROCHLORIDE

ITS USE IN THE MANAGEMENT OF INSTITUTIONALIZED GERIATRIC PATIENTS

Fred T. Darvill Jr., M.D., Sedro Woolley, Wash.

The effects of methylphenidate were compared with those of a placebo in 70 senile patients committed to a state institution because of mental disturbances. Neither the patients nor those who rated their behavior (orientation, appetite, continence, cooperativeness, activity, rationality, personal care, and irritability) knew whether a given patient was receiving the drug or the placebo. Among those who received the drug, two dosage schedules were used, the doses being increased weekly until some patients were receiving 60 mg. daily during the sixth week of the study. No significant differences were found between the test and contratest groups as regarded weight, pulse rate, or behavior ratings. A statistically significant lowering of the blood pressure was found among the subjects who received a maximum daily dose of 30 mg. of methylphenidate but was not found among those who received the maximum daily dose of 60 mg. No undesired side-effects were observed in this study, but the drug in the dosages used did not have any convincing effect on the physical or mental status of the patients.

Methylphenidate (Ritalin) hydrochloride, a psychotropic amine, has been evaluated as to its effect in a variety of psychiatric conditions, including depressions of the aged,[1] severe regression,[2] and schizophrenia.[3] Control groups were used in these studies. Benefit was reported in the first two of the above groups as a result of administration of this drug.

Dube and co-workers[4] evaluated 20 senile patients utilizing a double-blind technique and reported that methylphenidate in a dosage of 10 mg. given four times a day definitely improved behavior when compared to reserpine (1 mg. daily) or to placebos. Patients so studied served as their own controls. However, the number of patients studied is too few to permit drawing other than tentative conclusions.

Ferguson and Funderburk[5] have reported methylphenidate to be of value in the management of primarily retarded committed geriatric patients. Davidoff and associates[6] gave the drug to 10 geriatric patients and reported good results in 6. Side-effects (tension and insomnia) were seen in six patients and were especially evident in those who did not show improvement while receiving the drug.

The latter two studies did not use control groups. The rating of subjective phenomena depending primarily on the judgment of the investigators is known to be unreliable and the results subject to question unless the study is carried out with the double-blind technique.[7] This is particularly true in investigating senile behavior, where any degree of attention or interest will frequently result in an improvement in the parameters being evaluated.[8] To date, no serious effect in any organ or system or in blood pressure or pulse rate has been noted with the use of this drug.[9]

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After reviewing the above papers it was felt worthwhile to evaluate the effect of this drug on senile behavior in a controlled fashion, with use of a sufficient number of patients to allow accurate statistical evaluation. Accordingly, a double-blind evaluation of methylphenidate in the management of institutionalized geriatric patients was undertaken.

Method of Study

All patients studied in this series were committed to Northern State Hospital, Sedro Woolley, Wash., by the superior courts of the state of Washington. Sixty of the subjects who completed the course of study were selected from newly admitted patients, 60 years of age and older, sent directly to the medical geriatric admission ward.[10] All newly admitted patients had a complete history and physical examination and a mental status examination; laboratory studies included a white blood cell count, hematocrit value determination, urinalysis, blood urea nitrogen level determination, serologic tests for syphilis, chest x-ray, and electrocardiogram. After the above evaluation was completed, all patients who were diagnosed as having chronic brain syndrome due to cerebral arteriosclerosis or to senility were considered for the study. A study of higher priority was being conducted simultaneously which required the rejection of patients found to have the following physical conditions: angina, past or present; previous myocardial infarction; congestive heart failure, past or present; diabetes mellitus requiring insulin or tolbutamide therapy; chronic renal disease manifested by a blood urea nitrogen level of over 40 mg. %; diastolic hypertension manifested by a sustained diastolic pressure of over 110 mm. Hg; adrenal cortical hypofunction (Addison's disease); and peripheral vascular insufficiency of severe nature. The 60 newly admitted patients finally selected for this study all had one or more of the above physical disabilities; it can be seen, then, that these patients included in this study had poorer physical health than the average geriatric patient admitted to this hospital. Further indication of this selection was the fact that the average age of the patients in this group was 78 years, whereas the over-all average age of the geriatric patients was 74 years on admission.

Ten of the patients who completed the course of study were long-term occupants of geriatric wards. These patients were not screened on the basis of physical disease or laboratory findings and therefore represented the average geriatric patient as far as physical health and metabolic status was concerned. Five additional patients were started on this study but did not complete the eight-week course for reasons to be detailed later.

After a minimum of 10 days of hospitalization, the weight, pulse rate, and blood pressure were determined and the following eight parameters evaluated: orientation, appetite, continence, cooperativeness, activity, rationality, personal care, and irritability. A word description of the baseline state was then entered on the patient's rating sheet. These ratings were made in conference with the ward nurse, the ward physician, the attending staff, and the investigating physician. With the case number used as the sole criterion, these patients were then assigned alternately to either drug A or drug B, one of which was of methylphenidate, 10 mg., and one of which was a physically indistinguishable placebo. No one in the institution was aware of which drug was the active one and which was the placebo. No effort was made to assign patients to the study because of the degree of mental defect present, the degree of activity or retardation, or the findings in any of the evaluated parameters.

In 30 patients (group 1), 24 men and 6 women aged 65 to 91 years, the dosage was as follows: first week, one tablet daily; second week, one tablet twice a day; third to sixth weeks, one tablet three times a day; and, seventh to eighth weeks, no medication. For those patients who received the active drug, the dosage was 10 mg. daily the first week; 20 mg. daily the second week; and 30 mg. daily for the third to sixth weeks.

In 40 patients (group 2), 22 men and 18 women aged 65 to 98 years, the dosage was as follows: first week, one tablet daily; second week, one tablet twice a day; third week, one tablet three times a day; fourth week, one tablet four times a day; fifth week, one tablet five times a day; sixth week, two tablets three times a day; and, seventh to eighth weeks, no medicaments. For those who received the active drug, the dosage was 10 mg. daily the first week and weekly increments of 10 mg. daily were given for the next five weeks, so that the dose on the sixth week of the study was 60 mg. daily.

Toward the end of each of the eight weeks the blood pressure, pulse rate, and weight were again determined and the eight behavior parameters were reevaluated by the same rating team and compared to the base line on the following scale: much improved, some improved, no change, worse, and much worse. At the conclusion of the eight-week period an over-all evaluation of the response to therapy was made, both in words and with the rating scale. Any medical diseases or additional behavioral manifestations occurring during the study were noted.

Results

Of the 75 patients at the start of this study, 70 completed the eight-week course of medication and observation. Two patients, one receiving methylphenidate and one receiving the placebo, died suddenly during the study. Clinically, these deaths were presumed to be due to coronary artery disease. One patient receiving methylphenidate had a cerebral vascular accident which necessitated cessation of oral drug therapy. One patient receiving the placebo became so agitated that emergency electroshock therapy was imperative. One patient was dropped from the study for treatment of hypothyroidism bordering on myxedema which was suspected clinically but not confirmed before the study was instituted.

In the 30 patients completing the study in group 1, there were no significant medical illnesses occurring in those patients who received methylphenidate. Among those given the placebo, a carbuncle, one case of pneumonia, and one case of paroxysmal supraventricular tachycardia appeared. Of the 40 patients in group 2, one case of bronchitis, one case of lethargy, and one grand mal epileptic seizure were noted in the patients treated with methylphenidate. Two cases of pneumonia and one case of congestive heart failure were noted in the placebo group.

Over-all Response to Methylphenidate and Placebo Therapy in Geriatric Patients

	Much Improved, No.	Some Improved, No.	No Change, No.	Some Worse, No.	Much Worse, No.
Group 1					
Placebo	2	5	7	1	0
Methylphenidate	2	3	8	2	0
Group 2					
Placebo	1	6	10	3	0
Methylphenidate	2	4	12	1	1

No significant changes occurred in weight or pulse rate in either the experimental or control group. In group 1 (but not group 2) a significant ($p=0.01$) reduction in blood pressure occurred in the group treated with methylphenidate, as compared to the group treated with the placebo.

No statistically significant differences in any of the evaluated parameters could be demonstrated between the experimental and control groups in either dosage range. No statistically significant difference could be detected in the over-all response between the experimental and control groups in either dosage range. The table details the over-all response in both groups.

Comment

It is apparent that, in this group of elderly, senile, institutionalized patients, methylphenidate in adequate doses was of no value in improving the senile state. The improvement noted on previous studies and in this study was most likely due to the increased attention and interest which the patients received when selected for study. The need to carefully control studies in evaluating drugs of all kinds, and particularly drugs which may improve or influence the senile state, is again demonstrated.

The blood pressure change noted in group 1 is interesting, and it is suggestive that this drug may conceivably act as an antihypertensive agent. However, no blood pressure change of significance was noted in group 2. Although the blood pressure changes noted were statistically significant, it seems probable that these changes were coincidental. Further study is needed in this regard.

Summary

Seventy senile, institutionalized patients were studied with use of the double-blind technique during treatment with methylphenidate (Ritalin) hydrochloride and an identical placebo. No significant toxicity was noted in two groups receiving different dosages. No statistically significant improvement in the senile state could be demonstrated as a result of such treatment with methylphenidate.

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The statistical evaluations were performed by Dr. B. M. Bennett, Department of Public Health and Preventive Medicine, University of Washington School of Medicine.

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MEPHENTERMINE SULFATE FOR TREATMENT OF ARTERIAL HYPOTENSION

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The possibility of using mephentermine sulfate to treat various types of hypotension was studied in three groups of patients. Group 1 consisted of 10 patients who had hypotensive episodes during a rigorous course of treatment for essential hypertension or hypertensive renal disease. Group 2 consisted of 10 patients who had hypotensive episodes related either to diabetes or to cerebral arteriosclerosis. Group 3 consisted of 10 patients with a variety of nonspecific hypotensive syndromes. Measurements of blood pressure, of maximum ventricular excursion by roentgenkymography, of the I-J wave in ballistocardiograms, of blood flow in the finger, and of peripheral vascular resistance showed that mephentermine in the dosages used corrected the hypotension by both central and peripheral action. It was active when given orally, intramuscularly, or intravenously. For the type of hypotension seen in group 2, a daily oral dose of 12.5 mg. after the morning or noonday meal usually sufficed.

Hypotension may be caused by or associated with diabetes, cerebrovascular insufficiency, and a miscellaneous group of other diseases commonly characterized by a tendency to lethargy, fatigability, daytime drowsiness, and postural dizziness. The same symptoms also are produced in a certain percentage of patients by the ganglion-blocking agents, although considerable research has been directed toward reducing the severity of this complication to antihypertensive treatment. Trimethidinium methosulfate, for example, one of the newer asymmetric bisquaternary compounds (fig. 1), which exerts a potent ganglioplegic activity, induces postural hypotensive symptoms in about the same incidence as do other ganglion blockers. Its formula is d-[N-methyl-N-(γ-trimethylammoniumpropyl)] 1-methyl-8,8-dimethyl-3-azobicyclo [3.2.1] octane dimethosulfate. Parenteral or oral dosage, in the usually recommended range, exerts ganglioplegic activity for approximately 12 hours.

Mephentermine sulfate (N,α,α,trimethylphenethylamine sulfate) is a sympathomimetic pressor amine. This compound produces an antiarrhythmic [1] and positive inotropic action and also vasoconstriction.[2] In dogs, coronary flow has been increased under constant coronary perfusion pressures.[3] Mephentermine may be administered orally or parenterally and has been used clinically for prevention or treatment of hypotension associated with spinal anesthesia [4] and for correction of depressed blood pressure associated with shock in myocardial infarction [5] and obstetric delivery.[6]

The present study was designed to determine the effectiveness of mephentermine in controlling an excessive hypotensive response to the ganglionic blocking agent, trimethidinium methosulfate, and management of hypotension in a variety of other conditions.

Methods and Materials

The series consisted of 45 outpatients 23 to 72 years old, with an average of 49 years. Eighty per cent were men.

Group 1 (table 1) comprised 10 patients (7 men and 3 women), with an average age of 48 years, who had essential hypertension or whose elevated blood pressure was caused by polycystic kidney disease, glomerulonephritis, or obstruction of the renal artery (Goldblatt's hypertension). Retinopathy of grade 2 or 3 severity, according to the Keith-Wagener criteria, was present in every case. All had been maintained on a low-sodium diet and had been receiving diuretics and Rauwolfia serpentina. Trimethidinium methosulfate also had been administered orally, on a fasting stomach, at intervals of 12 hours, for one to five months. Total daily dosages ranged from 40 to 120 mg., with an average of 60 mg. Under this regimen most of the patients obtained reduction in blood pressure but occasionally experienced postural hypotension three to four hours after the morning medication. When hypotensive symptoms occurred during the course of trimethidinium therapy, 30 mg. of mephentermine was administered intramuscularly; later a dose of 25 mg. was administered orally for each hypotensive episode. The blood pressure was then read at intervals for two hours.

Group 2 (table 2) consisted of 10 patients, 4 with diabetes and 6 with cerebrovascular insufficiency caused by arteriosclerosis. In these patients orthostatic hypotension was particularly troublesome during hot weather, during convalescence from infection or operation, and in the presence of fatigue. During hypotensive periods 25 mg. mephentermine was administered orally after breakfast each morning.

Of the 10 patients in group 3 who had nonspecific hypotensive syndromes, 4 had neurasthenia, 3 were suffering from malignant processes, 2 had chronic infections, and 1 was convalescing after operation.

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Orthostatic hypotension, with postural dizziness, depression, and lethargy, was episodic and aggravated by heat and fatigue. The control blood pressure with the patients standing averaged 92 mm. Hg systolic (range, 88 to 100) and 55 mm. Hg diastolic (range, 42 to 62). Mephentermine was administered orally, in a dose of 25 mg., after breakfast.

Determinations of Blood Pressure, Cardiac Output, and Pulse Volume.—Segmental and digital plethysmograms were taken with equipment previously described.[7] Roentgenkymograms were recorded with the Liebel-Flarsheim kymograph. Ballistocardiograms were taken with the Nickerson low-frequency standardized table. Blood pressure was determined with a mercury manometer or with the Colson automatic blood pressure recorder.

Orthostatic hypotension was arbitrarily defined as blood pressure, with the patient in the standing position, of 100 mm. Hg systolic or less and 60 mm. Hg diastolic or less.

Results

Group 1 (table 1).—After administration of mephentermine, a rise in blood pressure occurred for all patients in group 1, in both standing and supine positions. The highest pressure with the patient standing is listed for each in table 1. Most patients were symptomatically improved; weakness and dizziness were eliminated or diminished.

Table 1.—*Effect of Mephentermine on Orthostatic Hypotension Produced by Trimethidinium*

				Blood Pressure, Mm. Hg							
				During Trimethidinium Treatment				After IM Dose of Mephentermine			
				Supine		Standing		Supine		Standing	
Case No.	Age, Yr	Sex	Diagnosis	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
1	48	M	Essential hypertension	120	90	90	60	150	95	120	88
2	55	M	Essential hypertension	150	100	98	65	170	108	130	95
3	60	F	Essential hypertension	185	102	100	70	172	104	120	85
4	50	M	Essential hypertension	158	95	102	60	162	100	124	86
5	45	M	Essential hypertension	159	100	98	65	180	110	138	90
6	38	F	Essential hypertension	160	100	90	60	185	115	120	88
7	39	M	Polycystic kidney disease	149	101	90	70	160	102	148	98
8	44	M	Glomerulonephritis	128	98	98	72	148	99	140	90
9	48	F	Glomerulonephritis	128	85	99	62	130	90	120	82
10	50	M	Obstruction of renal artery	138	90	100	70	140	100	128	99
Mean	47.7	M-7; F-3		147.5	96.1	96.5	65.4	159.7	102.3	128.8	90.1
Minimum				120	85	90	60	130	90	120	82
Maximum				185	102	102	72	185	115	148	99

The blood pressure response of the patient in case 6 is shown in figure 2. The hypotension was demonstrated by segmental plethysmographic record taken from the arm (fig. 3). With the patient in the supine position, the arm cuff was inflated to 100 mm. Hg (pressure at which the maximum pulsation was obtained). The blood pressure was 160/100 mm. Hg; the amplitude of the pulse curve was 0.6 cc. per pulse. As soon as the patient assumed the standing position, with the same pressure in the cuff, the amplitude was 0.1 cc. per pulse. On prolonged standing the amplitude of pulsation was reduced. One hour after intramuscular administration of 30 mg. of mephentermine the cuff was inflated to 115 mm. Hg (pressure at which the maximum pulsation was obtained). With the patient supine, the blood pressure was 185/115 mm. Hg and the pulse volume 0.93 cc. per pulse. As soon as the patient stood, the pulsation was reduced to 0.5 cc. per pulse and the blood pressure to 120/80 mm. Hg.

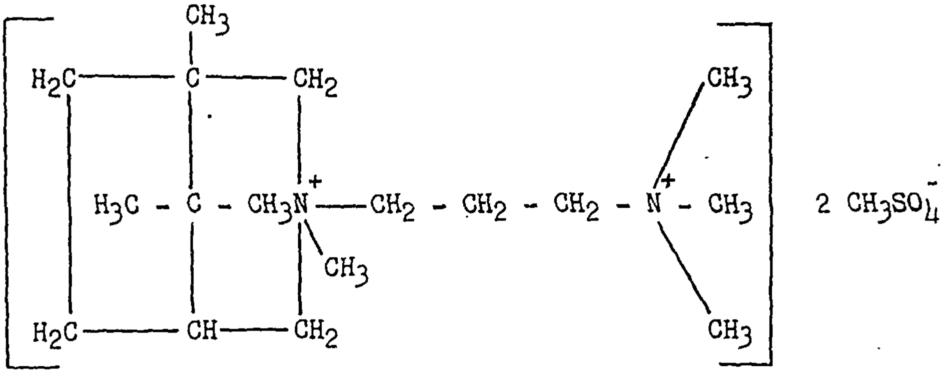

Fig. 1.—Trimethidinium methosulfate.

Group 2 (table 2).—A definite increase occurred in systolic and diastolic blood pressure with the patients standing as well as in the supine position. Three patients reported that they experienced less dizziness on standing, two were less fatigued during the day, three had less daytime drowsiness, and two reported subsidence of depression. On the 25-mg. dose, two patients reported nervousness and two insomnia and one each experienced quivering, vertigo, and nausea. For these the dose was reduced to 12.5 mg., after which there were no side-effects. Five of the group continued taking mephentermine in daily doses of 12.5 mg. for four months. A satisfactory antihypotensive action was maintained throughout this period; no tachyphylaxis occurred.

Figure 4 shows the effect of mephentermine on the blood pressure of the patient in case 17 (table 2) after an oral dose of 12.5 mg. taken in the fasting state. The blood pressure rose from 110/68 to 118/73 mm. Hg. Similar results were obtained in five patients (table 1) whose blood pressure was determined with the Colson recorder.

TABLE 2.—*Effect of Mephentermine on Orthostatic Hypotension Associated with Diabetes and Cerebrovascular Insufficiency*

				Blood Pressure, Mm. Hg							
				Control				After Oral Dose of Mephentermine, 25 Mg.			
				Supine		Standing		Supine		Standing	
Case No.	Age, Yr.	Sex	Diagnosis	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
11	34	F	Diabetes	110	80	100	79	114	82	110	80
12	29	F	Diabetes	119	82	100	75	122	88	115	80
13	68	M	Diabetes	112	72	98	70	122	80	120	79
14	70	M	Diabetes	119	80	100	71	134	88	120	82
15	62	F	Cerebrovascular insufficiency	100	65	95	58	120	72	112	76
16	60	M	Cerebrovascular insufficiency	98	64	90	55	110	79	108	79
17	58	M	Cerebrovascular insufficiency	110	68	96	59	128	80	120	75
18	47	M	Cerebrovascular insufficiency	108	72	95	60	124	76	118	70
19	50	M	Cerebrovascular insufficiency	100	65	95	60	114	74	110	70
20	42	M	Cerebrovascular insufficiency	102	68	98	68	118	78	110	74
Mean	52.0	M-7; F-3		107.8	71.6	96.7	65.5	120.6	79.7	114.3	76.5
Minimum	29			98	64	90	55	110	72	108	70
Maximum	70			119	82	100	79	134	88	120	82

Group 3.—One hour after the oral dose of mephentermine the systolic blood pressure averaged 107 mm. Hg (range, 98 to 118) and the diastolic 64 mm. Hg (range, 52 to 78). For three patients the dose of mephentermine was reduced to 12.5 mg., since the 25-mg. dose seemed excessive and had induced some nausea or nervousness.

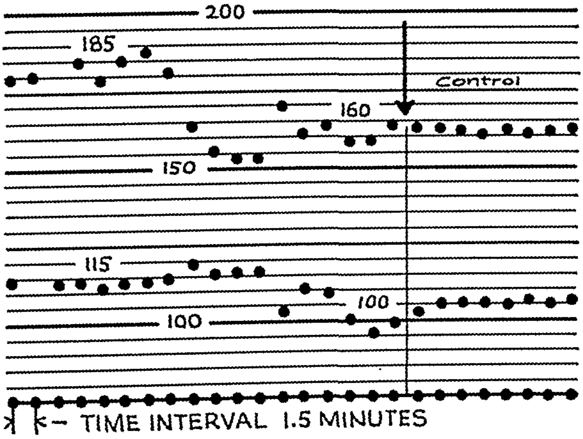

Fig. 2 (case 6).—Blood pressure of patients with severe essential hypertension. Postural hypotension occurred after administration of trimethidinium methosulfate and patient was dizzy on standing; hypotensive symptoms were controlled by intramuscular injection of 30 mg. of mephentermine. Arrow indicates time of injection. Read record from right to left.

Mechanism of Action.—The mechanism of action was studied by observing the effects of mephentermine on the heart, as recorded on the roentgenkymogram and the ballistocardiogram, and on the peripheral circulation by determination of the finger blood flow and local peripheral resistance.

A roentgenkymogram was taken for five patients. The maximum amplitude of pulsation of the left ventricular border was recorded before administration of mephentermine and one hour after intramuscular injection of 25 mg. (table 3). The studies made before antihypotensive medication were done during episodes of orthostatic hypotension. The roentgenograms were taken with the patient in the standing position. A definite increase occurred in the amplitude of pulsation one hour after administration of the dose.

Ballistocardiograms were taken for five patients, three with diabetes and two with cerebrovascular insufficiency (table 4). All had a tendency toward hypotension in the supine position. The height of the I-J wave was measured in millimeters before administration of mephentermine and one hour after intramuscular injection of 25 mg. In all cases the amplitude of the I-J wave increased after the injection.

TABLE 3.—*Mechanism of Action of Mephentermine for Correction of Hypotension: Results of Roentgenkymography of Chest*

		Maximum Excursion Left Ventricle (Mm.)	
Case No.	Diagnosis	Before Mephentermine	After IM Dose of Mephentermine, 25 Mg.
21	Diabetes	3.0	4.0
22	Diabetes	2.5	3.5
23	Diabetes	2.5	3.5
24	Cerebrovascular insufficiency	3.0	4.5
25	Cerebrovascular insufficiency	2.5	3.5
Mean		2.7	3.8
Minimum		2.5	3.5
Maximum		3.0	4.5

Finger flow and peripheral resistance were measured in five patients, three of whom had Raynaud's disease, for which sympathectomy affecting the upper extremities had been done. Two had thromboangiitis obliterans. The blood pressure was recorded by the auscultatory method, with use of a mercury manometer at the elbow. Finger flow was determined with a vein-occluding digital cuff. Peripheral resistance was calculated by taking the sum of the systolic blood pressure and twice the diastolic pressure, dividing by 3 to obtain the mean arterial pressure, and inserting this figure into the formula, as follows: Mean pressure in millimeters of mercury÷blood flow in cubic millimeters per 4 cc. of digit per second=the peripheral resistance units (PRU).

Comment

The positive inotropic action of mephentermine has been demonstrated by Freiheit[8] and others.[9] Oppenheimer[10] has shown that this compound decreases the refractory period and increases the conduction velocity in the cardiac muscle. A peripheral effect of mephentermine is suggested by the beneficial action of the compound when it is used in conjunction with spinal anesthesia.[4]

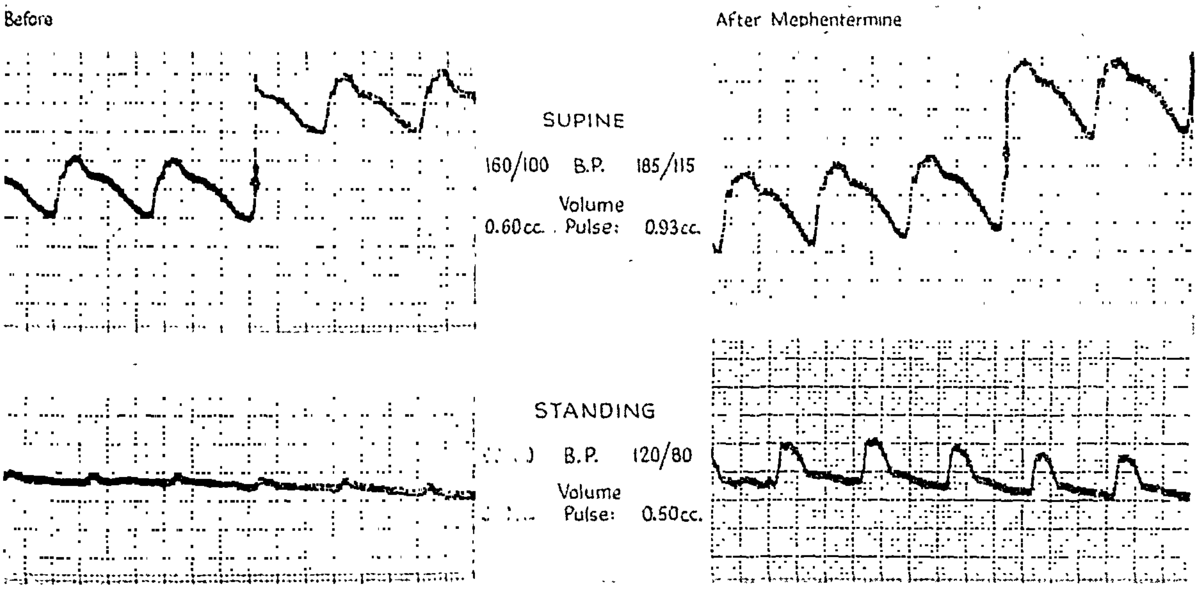

Fig. 3 (case 6).—Pulse volume in arm before and after administration of mephentermine. Standardization represents volume change of 1 cc.

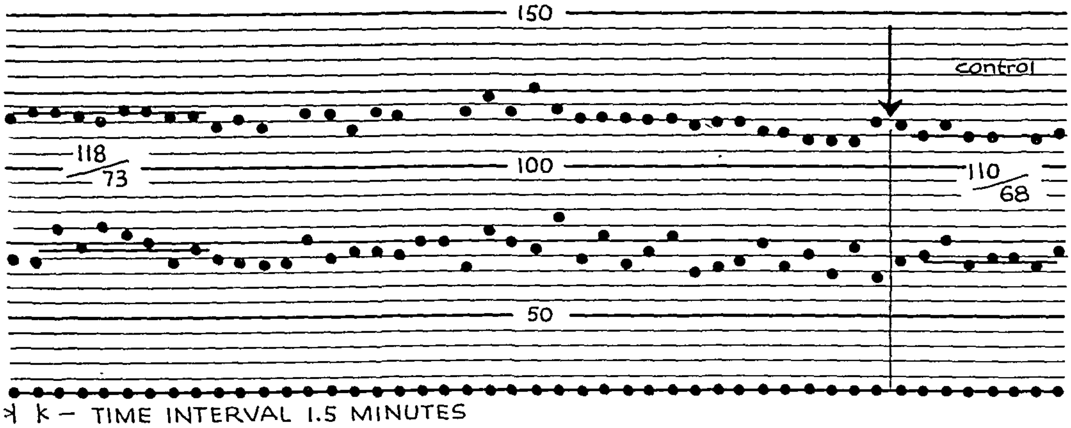

Fig. 4 (case 17, table 2).—Effect on blood pressure of oral dose of 12.5 mg. of mephentermine administered on fasting stomach (read from right to left).

Measurements made before administration of mephentermine and one hour after intramuscular injection of 25 mg. showed decrease in blood flow with increase in peripheral resistance (table 5).

As a result of the antihypotensive medication, there was a definite decrease in the amplitude of pulsation in the digit from an average of 2.0 to 0.5 cu. mm. per pulse. A typical record is that of the patient in case 32 (table 5), which is shown in figure 5.

The findings in this study indicate that mephentermine is useful for correction of hypotension from various causes and that the mechanism of action is both central and peripheral. The excursion of the left ventricular pulse and the force of the cardiac contraction were increased, and there was a mild increase in the local peripheral resistance and decrease in the amplitude of the pulsation at the fingertip. A positive inotropic and a peripheral action were induced by intramuscular injection of

25 mg. of the compound. This dose is small in comparison with that used for reversal of acute shock in myocardial infarction. In such cases an initial intramuscular or intravenous injection of 50 mg. is often required to return the blood pressure to normotensive levels.

The usefulness of mephentermine has been demonstrated for treatment of hypotensive episodes during medication with ganglionic blocking agents.

TABLE 4.—*Data from Ballistocardiogram Taken Before and After Intramuscular Injection of Mephentermine*

		Height of I-J Wave (Mm.)	
Case No.	Diagnosis	Before	After 25 Mg. IM
26	Diabetes	3.0	5.0
27	Diabetes	4.5	7.5
28	Diabetes	5.0	6.5
29	Cerebrovascular insufficiency	4.5	7.0
30	Cerebrovascular insufficiency	6.0	9.0
	Mean	4.6	7.0
	Minimum	3.0	5.0
	Maximum	6.0	9.0

When symptoms of postural hypotension are severe the compound should be administered intramuscularly or intravenously. For mild symptoms the oral form is adequate.

Hypotension associated with diabetes or cerebrovascular insufficiency often can be treated adequately with a daily oral dose of 12.5 mg. of mephentermine, administered after breakfast. This dose is well tolerated, appears not to produce tachyphylaxis, and is usually sufficient to support the blood pressure of patients who exhibit a nonspecific hypotensive syndrome.

Since mephentermine exerts a prolonged activity (e. g., in this series a dose of 12.5 to 25 mg. sufficed for 12 to 24 hours), the compound should not be taken later than 4 p. m. because of the possibility of insomnia. The larger the dose, the longer is the action and the greater the tendency toward sleeplessness. In properly adjusted dosage, mephentermine medication may be continued indefinitely.

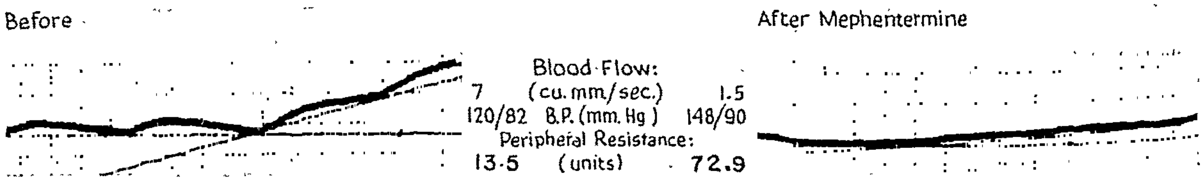

Fig. 5 (case 32, table 5).—Effect of mephentermine on finger blood flow and peripheral resistance.

Summary

Hypotension may be caused by or associated with a variety of diseases in which abnormality of the cardiovascular system is involved and may attend use of the ganglionic blocking agents. Mephentermine sulfate was given intramuscularly to 45 adult patients to correct an excessive response to use of trimethidinium methosulfate and orally, after a meal, to control hypotension associated with diabetes, arteriosclerotic cerebrovascular insufficiency, and a variety of nonspecific hypotensive syndromes.

The cardiac output, pulse volume, and peripheral resistance were measured by segmental and digital plethysmograms, roentgenkymograms, and ballistocardiograms; the blood pressure was recorded with a mercury manometer or the Colson automatic recorder. Orthostatic hypotension was defined as systolic pressure of 100 mm. Hg or less and diastolic pressure of 60 mm. Hg or less with the patient in the standing position.

TABLE 5.—*Finger Blood Flow and Peripheral Resistance Before and After Intramuscular Injection of Twenty-five Milligrams of Mephentermine*

		Brachial Blood Pressure, Mm. Hg		Finger Flow, Cu. Mm./4 Cc./Second		PRU*	
Case No.	Diagnosis	Before	After	Before	After	Before	After
31	Raynaud's disease	130/70	150/85	14	2.0	6.4	53.3
32	Raynaud's disease	120/82	148/90	7	1.5	13.5	72.9
33	Raynaud's disease	128/82	158/98	12	1.0	8.1	118.0
34	Thromboangiitis obliterans	110/68	150/92	19	4.0	4.3	27.8
35	Thromboangiitis obliterans	118/78	160/102	24	6.0	3.8	20.3
	Mean	121/76	153/93	15.2	2.9	7.2	58.5
	Minimum	110/70	148/85	7	1.0	3.8	20.3
	Maximum	130/82	160/102	24	6.0	13.5	118.0

* PRU = Peripheral resistance unit.

Intramuscular injection of 25 to 30 mg. of mephentermine sufficed to counteract the excessive response to a ganglionic blocker. For mild symptoms the orally given form was adequate. For hypotension associated with diabetes, cerebrovascular insufficiency, or other conditions, a daily oral dose of 12.5 mg. after a meal was sufficient; for severe symptoms 25 mg. might be required. In properly adjusted dosage, mephentermine medication may be continued indefinitely.

The mechanism of action of mephentermine is both central and peripheral. Intramuscular injection of the compound produces a positive inotropic action and induces a mild increase in local peripheral resistance with decrease in the amplitude of the pulsation at the finger tip. The pressor activity is prolonged; hence, the dose should not be administered after 4 p. m. because of the possibility of insomnia.

3875 Wilshire Blvd. (5).

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Sally Cody supplied technical assistance in this study.

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CLINICAL NOTES

SWEAT BAND DERMATITIS—REPORT OF THREE CASES

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Sweat band dermatitis has not recently been described in the medical literature of the United States, and one of the underlying reasons for its low incidence is the fact that chrome-tanning compounds are not used in the preparation of sweat bands. Therefore, the leather of sweat bands contains, if any, only a limited amount of chromium. The vegetable tannins which are used are not potent sensitizers.

The use of chrome-tanned leather in sweat bands obtained under its procurement program has been specifically prohibited by the United States government in the two pertinent specifications which are now in force. "Military Specification MIL-B-3577A (S&A), Jan. 19, 1954, Band, Sweat, Cap (Leather)," which covers the requirements for sweat bands used in caps worn by military personnel, states that "chrome-tanned leather will not be permitted." "Interim Federal Specification GG-H-00166a (GSA-FSS), April 18, 1956, Headbands, Mirror," which covers mirror headbands for use by practitioners and specialists, states that "the leather shall be well tanned with vegetable tanning materials."

These governmental restrictions, as well as the self-imposed restrictions of the larger manufacturers of sweat bands in the United States, against the use of chrome-tanned leather now appear to have been in the best interests of the public. For it has now been established [1] that the lactic acid and lactate portions of human perspiration can leach chrome salts from chrome-tanned leather and deposit them onto the skin and that sensitization dermatitis can result from the basic chromic sulfate—$[Cr(H_2O)_5OH]\ SO_4$—thus deposited on the skin. Considering the uniquely close contact of the sweat band with the forehead, it would have been inevitable, had these restrictions not been in effect, that some persons would have developed dermatoses from this trivalent chromium sensitizer. This basic chromic sulfate is not related to either chromates or dichromates, as is evident from figure 1. The soluble chromates and dichromates form yellow and orange solutions for the most part, whereas the basic chromic sulfate salt found in chrome-tanned leather forms a green solution.

This basic chromic sulfate compound is now available for patch-testing purposes and has caused positive patch-test reactions in a 0.2% solution.[1] It is the chemical that should be used if one suspects

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that the chromium of the leather is the cause of a person's dermatitis. There is neither chromate nor dichromate in shoe leather. The leaching of basic chromic sulfate by the lactic acid and lactate portions of the perspiration has caused dermatoses of the hands and feet from the wearing of chrome-tanned leather gloves and shoes in sensitized persons.[2]

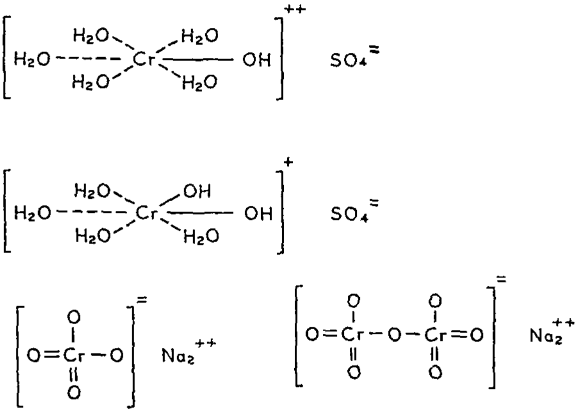

Fig. 1.—Formulas of complex coordination compounds found in a chrome-tanned leather: (*top*) one-third basic; (*center*) two-thirds basic; (*bottom left*) chromate ion; and (*bottom right*) dichromate ion.

Chemical analysis of a nurse's stockings (whose white shoes had shown green chrome-discoloration) has shown that they contained a considerable quantity of trivalent chromium salts. This is the first report of the finding of trivalent chromium salts in stockings. The sample was extracted in a Soxhlet extractor with water and the extract concentrated. A qualitative test for hexavalent chrome was run with use of diphenylcarbazide as a reagent. This test gave negative results. A portion of the extract was then dried down and oxidized to the hexavalent form and the diphenylcarbazide test repeated. In this case there was a very strong positive reaction for hexavalent chrome. This means that in the stocking there was practically a complete absence of hexavalent chrome but a considerable quantity of trivalent chrome.

Chromium salts, however, are rarely used in the tanning of sweat bands in the United States, and the only recent cases of sweat band dermatitis that have been reported (both were in the foreign literature) have been described as being due to Thioprene latex used as a sizing agent in paper or cloth sweat bands[3] or as being due to a laurel oil with which some hats are treated.[4]

This report deals with three cases of typical sweat band dermatitis seen in my practice, one from paper and the other two from rubbing substances onto the sweat band by the hands.

Report of Cases

Case 1.—A worker in a cordage plant developed a generalized dermatitis (extending from his neck to his feet) from the oiled fibers of the rope. He was kept out of work, given treatment, and completely cleared of his eruption. He was told to destroy all his old clothing, and new protective clothing was supplied. He returned to work and was seen one week later with a dermatitis of the sweat band area. The only article of clothing he had not discarded was an old hat that he was accustomed to wear at work. He volunteered the information that over a period of months he was in the habit of wiping the accumulated sweat off the sweat band with his oily hands, and it was evident that the band had thus become saturated with oil. When he wore the hat subsequently, the oil caused an eruption on his forehead, although it had not done so at the time of his previous eruption. Oil was extracted from the sweat band with ether; the ether was then evaporated; and the patient had a positive reaction to the residual oil thus extracted from the sweat band.

Case 2.—This patient was employed as a painter and wore the typical painter's hat. The sweat band was a piece of paper impregnated with a sizing material, the nature of which could not be determined. After he had worn the hat some months, a typical crusted sweat band dermatitis ensued. There was a sharp outline of erythema, with scaling and hemorrhagic crusting encircling the head where the sweat band contacted the skin. A patch test to the paper gave positive results after 24 hours. The man was given treatment.

Case 3.—A worker in a tannery had suffered from a dermatitis from a tanning solution over a period of 10 years. During the last eight months it had been spreading. On examination, he showed a papular eruption of the arms, forearms, and hands, parts of his body in immediate contact with the solution, and similar dermatitis in areas about the knees where splashes of the chemical came in contact with his clothing above the high boots that he wore. He had a rash of the sweat band area, where he said he had been wiping the perspiration off of the sweat band.

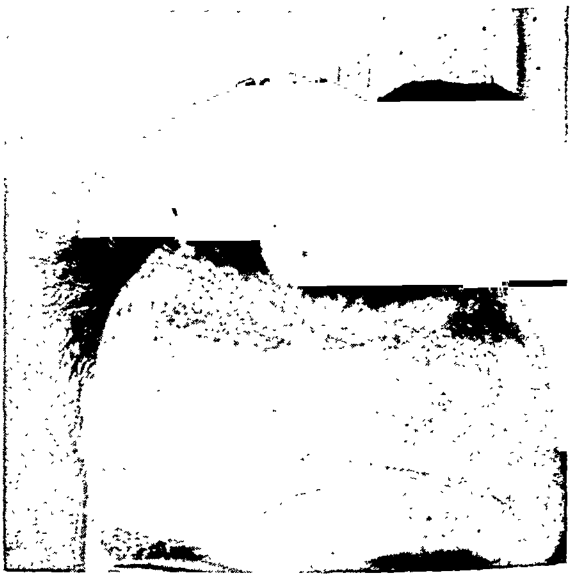

Fig. 2 (case 2).—Typical case of sweat band dermatitis.

Summary and Conclusions

Chrome-tanned leathers are not used in sweat bands. This is the first report that trivalent chromium salts have been found in stockings. Basic chromic sulfate is a cause of dermatitis among sensitized persons. Sweat band dermatitis is not common. However, the diagnosis is simple, and the cause may be the finishing material of synthetic fibers or of paper dissolved onto the skin by perspiration or it may be due to substances rubbed onto the sweat band by the hands.

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SHOCK AFTER ADMINISTRATION OF PROCHLORPERAZINE IN PATIENT WITH PHEOCHROMOCYTOMA

REPORT OF A CASE WITH SPONTANEOUS TUMOR DESTRUCTION

Irwin A. Brody, M.D., Durham, N. C.

Severe hypotension after administration of chlorpromazine is not common. Conventional doses may sometimes induce a moderate fall in blood pressure, but this is not usually sufficient to cause symptoms.[1] I have recently observed the sudden development of shock after administration of 10 mg. of prochlorperazine (Compazine) ethane disulfonate intramuscularly to a patient with a subsequently proved pheochromocytoma. This episode was followed by loss of function of the tumor. The purpose of this case report is to suggest that patients with pheochromocytomas may be unusually susceptible to the hypotensive effects of phenothiazine derivatives and that the occurrence of shock in this patient may have precipitated the degeneration of the tumor.

Report of a Case

An 18-year-old girl was admitted to Duke Hospital on July 25, 1958, for evaluation of recurrent abdominal pain. She had had headaches for six months, induced by exertion and relieved soon after lying down. Four weeks prior to admission she began to have recurrent attacks of generalized abdominal "pain" lasting about 30 minutes and often accompanied by vomiting. During the week preceding admission she had developed exertional dyspnea and orthopnea. Her health had previously been good. On physical examination her weight was 75 lb. (34 kg.); temperature, 101.4 F (38.6 C); pulse, 128 per minute; and blood pressure, 190/150 mm. Hg. The arterial pressure showed an orthostatic fall to 130/110 mm. Hg, and the pulse rate increased to 140. Her skin was pale and dry; the ocular fundi showed arteriolar spasm, venous compression, hemorrhages, and exudates. Neck veins were moderately distended. Examination of the heart revealed a loud split-second pulmonic sound; a harsh systolic murmur, accompanied by a thrill, was heard at the second left parasternal space. The liver was palpable just below the right costal margin. There was mild right costovertebral angle tenderness but no peripheral edema.

Laboratory studies on the blood showed hemoglobin level, 9.4 Gm. per 100 cc.; hematocrit value, 36%; red blood cells, hypochromic; white blood cells, 15,960 per cubic millimeter. Urine showed a trace of protein, a trace of sugar, and was otherwise normal. The fasting blood sugar level was 121 mg. per 100 cc. and the nonprotein nitrogen level 27 mg. per 100 cc. Urine and blood cultures showed no growth. The electrocardiogram showed isolated T-wave negativity from V_2 to V_4. X-ray studies showed that the heart was at the upper limits of normal in size and the lungs were clear. An intravenous urogram demonstrated prompt excretion of the dye, but the right kidney was displaced downward.

Hospital Course.—The patient remained febrile but felt well until the fourth hospital day when she suddenly developed severe abdominal cramps and vomiting. Four hours later 10 mg. of prochlorperazine was administered intramuscularly to allay her symptoms. The patient's blood pressure fell within 10 minutes from 190/150 to 80/60 mm. Hg, and she had the clinical appearance of shock. She was placed immediately in the Trendelenburg position and levarterenol (Levophed) bitartrate was administered by intravenous drip. After five hours her blood pressure had stabilized at 120/80 mm. Hg and the levarterenol was discontinued. During the next 24 hours her blood pressure rose to a new level of 160/120 mm. Hg. The abdomen remained diffusely tender and distended without guarding and intestinal sounds were hypoactive.

By the seventh hospital day, about 96 hours after its onset, abdominal pain had subsided and the patient tolerated oral feedings. Thereafter she had only minor attacks of "pain." Her temperature gradually declined to normal by the 13th hospital day, and the intensity of her cardiac murmur diminished. Her blood pressure, which had remained at 160/120 mm. Hg during her period of severe pain, slowly decreased to 100/70 mm. Hg by the 16th hospital day. Intravenous administration of 5 mg. of phentolamine (Regitine) hydrochloride on the 11th hospital day produced a fall in blood pressure from 166/120 to 98/62 mm. Hg within 2 minutes, with a return to pretest levels within 10 minutes.

Urinary catechol amines were measured in the laboratory of Dr. M. Goodall by a bioassay utilizing cat's blood pressure and hen's rectal cecum.[2] The fluorometric method of Von Euler and Floding[3] was also used. The significantly elevated values of the 7th and 13th hospital days fell to normal by the 21st day (see table). Seventy-two hours elapsed between the

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end of the levarterenol infusion and the beginning of the first urine collection. This time interval seems long enough to preclude the possibility that exogenous norepinephrine (noradrenalin) was being measured in the urine.[4]

After normotension had become established a hypertensive response could be provoked neither by the intravenous administration of 200 mg. of tetraethylammonium (Etamon) chloride or of 100 mcg. of histamine base nor by vigorous massage of the right flank.

*Urinary Catechol Determinations—Micrograms per 24 Hours**

	Fluorometric		Bioassay	
Hospital Day	Epinephrine	Norepinephrine	Epinephrine	Norepinephrine
7	...	2,330.6	...	...
13	65.5	270.4	54.8	1,112.4
21	15.3	36.5	13.2	44.1
27 (Tumor removed)	...	...	...	...
41	17.9	29.5	3.2	31.8

* Average normal values [2]. epinephrine, 15.7; norepinephrine, 32.3

At laparotomy, on the 27th hospital day, a mass was found between the upper pole of the right kidney and the adrenal gland (see figure). This mass could be freed from the surrounding structures, but it was penetrated by the renal artery; consequently, the right kidney was excised after the renal artery was tied in removing the tumor. The adrenal gland was left intact. Throughout the procedure there was no significant change in blood pressure despite manipulation and removal of the tumor.

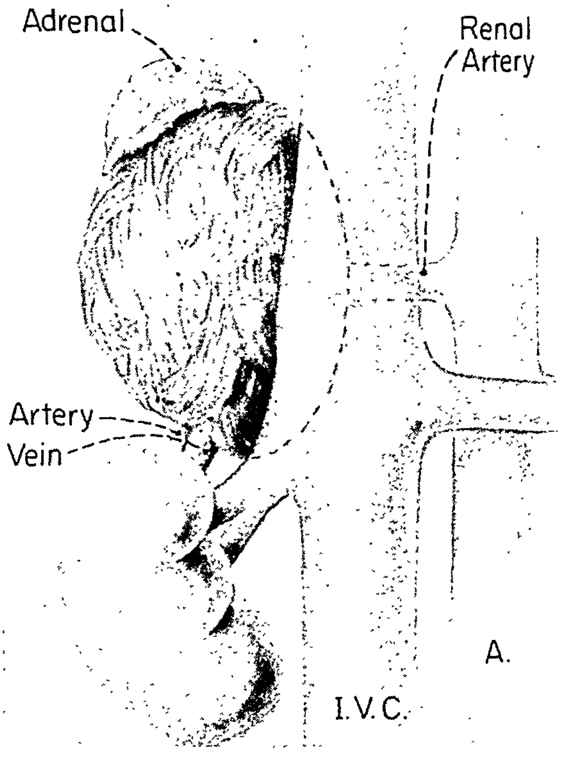
The patient's postoperative course was uneventful. She maintained a blood pressure of 110/80 mm. Hg and a pulse rate of 80 to 90 per minute, with orthostatic tachycardia. She felt entirely well on a return visit seven weeks after the operation, and her blood pressure was normal. Her eyegrounds showed complete resolution of the hemorrhages and exudates, and the arteriolar attenuation had disappeared.

Pathological Examination.—The gross specimen consisted of an encapsulated mass that weighed 5.4 oz. (153 Gm.) and measured 8 by 6.5 by 4 cm.; the capsule measured 7 mm. There was no connection with either the adrenal gland or the kidney. Cut section revealed that the tumor was yellowish brown, soft, and predominantly necrotic. Microscopic examination confirmed the impression of pheochromocytoma. There were no thrombi but the entire central mass was necrotic and had the appearance of an infarct. The infarcted area was organized from the periphery and among this fibrous tissue were small groups of chromaffin cells. Ghost-like cells in the necrotic center resembled these. The resected kidney appeared completely normal.

Comment

Phenothiazines and Shock.—The prompt development of shock in our patient after administration of prochlorperazine suggests that the drug precipitated her circulatory collapse. The pheochromocytoma may have predisposed her to this reaction or she may have been unusually sensitive to phenothiazines because of constitutional or other factors. An apparently normal individual rarely develops a marked fall in blood pressure in response to chlorpromazine.[1a] In our patient, however, another administration of 10 mg. of prochlorperazine intramuscularly seven weeks after the operation produced only a gradual, moderate decline in blood pressure without symptoms other than drowsiness, which made a constitutional basis for her severe hypotensive reaction appear unlikely. Hypertension itself does not seem to render a person more susceptible to shock induced by the phenothiazines. Stevenson and Sjoerdsma[5] studied the effect of intramuscular doses of 25 to 100 mg. of chlorpromazine in adults with benign essential hypertension and found no significant change in recumbent blood pressures.

On the other hand it seems that a patient with a pheochromocytoma, whose blood pressure is elevated by increased secretion of sympathetic amines, may be unusually sensitive to the hypotensive effects of the phenothiazines. There is much indirect evidence to support this view. Courvoisier and co-workers[6] found that chlorpromazine administered intravenously to dogs counteracted the pressor effect of infusions of norepinephrine and, to an even greater extent, of epinephrine (adrenalin). They stated that in large doses the effect of chlorpromazine resembled that of dibenzyl betachlorethylamine (Dibenamine) hydrochloride. Their animals were protected against a quantity of epinephrine equal to six times the lethal dose by the administration of 1 mg. of chlorpromazine per kilogram of body weight. Other studies have amply confirmed the adrenolytic properties of chlorpromazine.[7] Finkelstein and co-workers[8] showed that chlorpromazine in the fluid bathing an isolated heart muscle greatly reduced the positive inotropic action of epinephrine and norepinephrine.



Position of pheochromocytoma. Dotted lines show penetration by renal artery.

Although the adrenolytic effect of chlorpromazine might be the primary factor in causing a drop in the blood pressure of a patient with a tumor producing sympathetic amines, this response might be intensified by some of the other pharmacological actions of chlorpromazine, including depression of the vasomotor center,[9] ganglionic blockade,[10] and direct peripheral vasodilatation.[11]

A survey of the literature reveals only one description of a case of hypertension associated with pheochromocytoma in which the effect of administration of a phenothiazine derivative is discussed. Lima and co-workers[12] reported a patient in Brazil with a pheochromocytoma to whom 25 mg. of chlorpromazine was given intramuscularly for sedation during a hypertensive crisis. The blood pressure fell from 280/160 to 70/30 mm. Hg and a vasopressor agent was required. During subsequent paroxysms the administration of chlorpromazine was invariably followed by a prompt hypotensive response. When therapy was maintained with prophylactic oral doses of chlorpromazine the hypertensive crises became less frequent and intense.

The symptomatology often associated with a hypertensive paroxysm may prompt the physician to administer one of the phenothiazine analogs, or the symptoms may be interpreted as an acute anxiety syndrome requiring a tranquilizer. The diagnosis of pheochromocytoma should be considered if a severe hypotensive response follows the administration of the drug.

Pheochromocytoma and Shock.—Another feature of interest in this case is the apparent association of the hypotensive reaction to the degeneration of the tumor. The development of shock in a patient with a pheochromocytoma before surgical excision has been described.[13] In many of these instances the tumor appeared degenerated at operation or autopsy, and the peripheral vascular collapse was attributed to the destruction of the tumor with abrupt cessation of pressor hormone output.[14] In the case here presented it seems possible that the sudden development of shock was responsible for initiating or accelerating infarction of the tumor and that generalized circulatory failure was thus the cause of tumor necrosis rather than its consequence.

It is conceivable that some degree of local vasoconstriction is present within a tumor containing large quantities of norepinephrine. Hence the tumor, with its great metabolic demand, may suffer chronically from a relative deficiency of blood supply. The cystic and necrotic areas frequently seen on pathological examination of actively functioning pheochromocytomas[15] may be a reflection of this state. The sudden superimposition of generalized circulatory failure may then precipitate massive infarction in the already ischemic tissue, leading to progressive loss of its highly specialized function.

The sequence of events here proposed has not been considered in the available case reports of shock occurring in patients with pheochromocytoma. It is conceivable that drugs were the real cause of shock in some of these patients or that their shock was similar to the circulatory failure observed in animals infused with large doses of epinephrine.[16] However the shock was produced, the necrosis of the tumor may have been merely a secondary phenomenon.

The evidence for tumor degeneration in our patient rests not only on the profound morphologic changes but also on the disappearance of hypertension, the negative responses to the provocative tests, the decline to normal of the urinary catechol amine levels, the absence of a hypertensive response during manipulation of the tumor at surgery, and finally on the stability of the blood pressure after removal of the tumor. The functioning pheochromocytoma had become converted into a physiologically inactive mass, rendering the patient asymptomatic before surgical intervention. A similar demonstration of loss of function of a pheochromocytoma was not found in the literature.

Summary

In a case of pheochromocytoma the administration of prochlorperazine was followed by generalized circulatory failure and then by loss of tumor function, documented by successive catechol amine determinations. Patients with pheochromocytomas may be extraordinarily sensitive to the phenothiazine drugs, and shock after their administration might point to the diagnosis of pheochromocytoma when the clinical picture is otherwise unclear. It is suggested that an episode of shock may play a significant role in promoting necrosis of a pheochromocytoma.

The catechol amine determinations were made by Dr. M. Goodall and the pathological examination by Dr. Bernard F. Fetter. The operation was performed by Dr. George J. D'Angelo.

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ACUTE ALLERGIC COLITIS PRESENTING THE CLINICAL PICTURE OF ACUTE APPENDICITIS

REPORT OF A CASE

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This case report describes the effect of parenterally given epinephrine on colonic lesions in a case of acute colitis presenting the clinical picture of acute appendicitis.

A 47-year-old woman entered Beth Israel Hospital, Boston, on Sept. 1, 1955, with the chief complaint of abdominal pain of 24 hours' duration. The patient had been in good health until the evening before admission when, while sitting quietly, she noted the gradual onset of lower abdominal pain which became severe enough to cause fainting. The pain diminished somewhat but recurred; an analgesic was given subcutaneously for relief. The pain was described as cramping in nature with occasional severe exacerbations felt throughout the lower part of the abdomen. Between these exacerbations the patient noted a persistent ache in the lower part of the abdomen. She also experienced mild diarrhea. On the night prior to admission the patient had eaten lobster for dinner, as did several members of her family (no other members of the family were ill). Her history and a systemic review were completely negative except that the diagnosis of allergic rhinitis had been made in 1938.

Physical examination revealed a slightly obese, alert, cooperative female in no acute distress. Her pulse, respirations, and blood pressure were within normal limits, and the oral temperature was 99 F (37.2 C). Physical examination gave normal findings except for the presence of deep, right lower quadrant abdominal tenderness which could be demonstrated only with the patient in the right lateral decubitus position. Urinalysis revealed 1+ albuminuria. The white blood cell count was 19,600 per cubic millimeter. The diagnosis of acute appendicitis was made, and the patient was taken to the operating room.

At operation, performed by Dr. L. Hermansen, the cecum and transverse colon appeared normal, as did the sigmoid colon. However, a 12-cm. segment of the upper portion of the descending colon was involved in a bizarre reaction which ended abruptly at the junction of the descending colon and the sigmoid flexure; the entire intestinal wall was thickened and edematous but not discolored. Along the mesenteric borders of the intestine were numerous large bullae containing a clear fluid which was seen to extrude through the intestinal wall. The process resembled a local sensitivity phenomenon. Apparently the mesecolon and the adjacent peritoneum were not involved.

Biopsy was not deemed advisable. All fluid was aspirated from the bullae and 0.3 cc. of a 1:1,000 solution of epinephrine (Adrenalin) was administered parenterally with prompt partial regression of the process. Incidental appendectomy was performed, and the abdomen was closed in layers without drainage.

The postoperative course was benign, and the patient was discharged from the hospital on the sixth postoperative day. White blood cell counts prior to discharge from the hospital were normal and eosinophils were not present either in a differential smear or in an eosinophil count. Culture of the peritoneal fluid revealed no growth. The gross and microscopic examination of the appendix revealed a normal appendix. Routine scratch tests at the allergy clinic all gave negative results.

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Comment

Although mortality and morbidity from appendectomy have been reduced to extremely low levels,[1] there are many patients in whom it would be most desirable to avoid operation. In these patients one should use all available diagnostic techniques before scheduling even a "benign" surgical procedure. This report demonstrates the effect of epinephrine on acute bullous lesions of the serosal surface of the descending colon. As would be expected if the condition were allergic, these lesions regressed within minutes after the subcutaneous injection of epinephrine. It is, of course, impossible to correlate definitely the presence of these lesions with the clinical picture preoperatively, as it is also impossible to correlate the presence or absence ot these lesions with the lack of symptoms postoperatively. One can say only that (1) the only intra-abdominal pathology found at laparotomy were these bullous lesions, (2) the appendix was normal histologically, (3) these lesions regressed rapidly after epinephrine was given parenterally, (4) the patient had no symptoms postoperatively, and (5) the patient had a definite allergic history in the past. The clinical syndrome apparently was due, therefore, to some vague allergic factor which produced the bullous lesions and which was counteracted by parenterally administered epinephrine.

Allergic symptoms of the gastrointestinal tract have been reviewed extensively by Withers,[2] Andresen,[3] and Miller.[4] Andresen [5] describes three types of colonic syndromes which apparently have an allergic component: a mild reaction commonly called "mucous colitis" or "irritable colon"; a more severe reaction which he terms "colon spasm" or "colitis"; and a very severe reaction simulating intestinal obstruction, acute inflammation, or perforation. Andresen notes that in the very acute phase of the severe reaction ephinephrine chloride, 1 cc. or less of a 1:1,000 solution, will afford immediate and almost miraculous relief of symptoms. Eusterman [6] describes a patient with recurrent painful gastrointestinal allergy in whom subcutaneous injection of epinephrine relieved symptoms within 20 minutes. Merrill,[7] too, notes that epinephrine often is useful in treating gastrointestinal allergy. He describes a patient with acute abdominal distress who received epinephrine to combat initial shock with a lessening of her abdominal symptoms; subsequent laparotomy revealed changes in the terminal ileum and cecum which supported a diagnosis of allergy.

Although epinephrine or ephedrine sulfate administered subcutaneously or atropine given orally may relax allergic spasm and aid in differential diagnosis, Ratner [8] cautions that surgical intervention may be imperative despite an allergic component: a too pronounced or prolonged allergic reaction may develop into a condition amenable only to operation. Therefore, even in the face of an allergic background, if the signs resemble appendicitis or intussusception, surgical intervention may be imperative.

Had epinephrine been administered prophylactically, it is quite possible that in the patient reported here the symptoms would have disappeared or at least abated in much the same manner as the intestinal lesions did. Therefore, one might suggest a therapeutic trial with parenterally given epinephrine in patients presenting a clinical picture of acute appendicitis where a history of allergic disorder is present and especially where it would be desirable to avoid operation. The epinephrine should be given immediately and the patient observed closely while preparations for operation are in progress; then, if operation is required it need not be delayed.

A note of caution regarding the use of epinephrine: Needless to say, epinephrine should not be used in anyone in whom a specific contraindication for its use exists, but, equally important, the administration of epinephrine should not lull the physician into a false sense of security even if the signs and symptoms abate. The patient should be watched closely for a reasonable period of time so that any evidence of persistence or recurrence of symptoms may be detected immediately and appropriate steps taken before serious complications occur.

Summary

In a patient, bullous lesions of the serosal surface of the descending colon (presumably allergic in nature) regressed after the parenteral administration of epinephrine. A preoperative diagnostic test with parenterally given epinephrine may be done in such patients. This test will be of help in the differentiation of acute appendicitis from acute allergic colitis, and it should also reduce the frequency of unnecessary laparotomies.

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SPONTANEOUS RUPTURE OF AN ABDOMINAL AORTIC ANEURYSM INTO THE INFERIOR VENA CAVA

REPORT OF A CASE

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and
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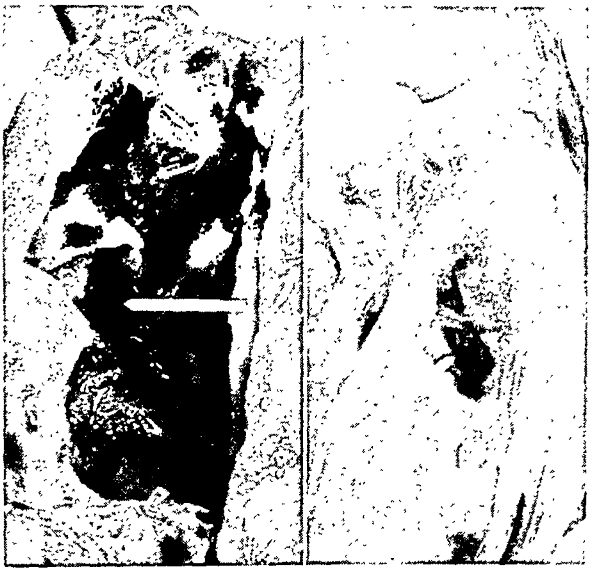
Although sporadic reports of arteriovenous fistulas between the aorta and inferior vena cava have been noted in the literature, these were the results of trauma, usually a gunshot wound. The spontaneous rupture of an abdominal aortic aneurysm into the inferior vena cava is a rare occurrence. Viar and Lombardo[1] reported in 1952 what they believed to be the first case. Their patient survived about six weeks after the development of such a spontaneous fistula, manifesting signs of severe progressive right heart failure, unresponsive to all medical therapy. Autopsy revealed a 13-cm. aortic aneurysm with a 1-cm. opening into the inferior vena cava.



Left, opening in arteriosclerotic aneurysm, revealing large fistula into inferior vena cava. *Right*, opening in inferior vena cava, revealing arteriovenous fistula.

More recently, Eiseman and Hughes[2] and Shumacker and Jontz[3] each described successful resection of an abdominal aortic aneurysm which had ruptured into the inferior vena cava and the replacement with a graft after closure of the caval defect. Both patients manifested severe cardiac failure, massive peripheral edema, widened pulse pressures, and pulsating abdominal masses with loud bruits. A case report describing some of the findings associated with this vascular catastrophe is given below.

A 69-year-old man, who had not been under prior medical care, was admitted on Nov. 23, 1956, with a six-hour history of severe abdominal pain followed by shock. Examination revealed an acutely ill elderly man with marked dyspnea and shallow respirations, pulse rate 120 per minute, and blood pressure 80/30 mm. Hg. The skin was cold and wet. Heart and lungs were within normal limits. A pulsating mass was present in the mid-abdomen and was associated with a to-and-fro murmur in this region and also along the vertebral spines posteriorly in the lumbar region. The pedal pulses were normal. Initial hemoglobin level was 13.1 Gm.%; his blood type was A positive. The initial impression was that a leaking abdominal aortic aneurysm was present. Emergency treatment consisted of nasally given oxygen and the infusion of 2 units of blood. The skin became warm and dry, but the rapid pulse and low blood pressure persisted. About three hours after admission he was taken to the operating room. During the induction of anesthesia he developed cardiac arrest. The left side of the chest was opened immediately through the fourth intercostal space, and cardiac massage was instituted. The heart developed ventricular fibrillation which was successfully defibrillated with the electric defibrillator. Cardiac massage was continued, but a satisfactory cardiac rhythm could not be reestablished.

Autopsy revealed a large fusiform aneurysm of the abdominal aorta arising about 2 cm. beyond the origin of the renal arteries. The aneurysm measured 10 cm. in diameter, and it extended downward to the bifurcation (see figure). The aneurysm was partially filled with pale, yellow-tan, laminated thrombus measuring up to 3 cm. in thickness. This thrombotic layer was thinnest in the right posterior portion adjacent to the vena cava. In the center of this area the thrombus was eroded, and the attenuated aneurysm wall had ruptured through the wall of the inferior vena cava, producing an arteriovenous fistula which measured slightly more than 2 cm. in its greatest diameter. There was no evidence of rupture into the retroperitoneal space. The other regions of the aorta showed considerable arteriosclerotic changes in the ascending portion, arch, and major branches. The coronary arteries also showed extensive arteriosclerosis with calcification but no serious impairment of the lumen. The remainder of the autopsy showed essentially normal findings.

Microscopic examination of the aorta in the region of the fistula revealed extensive infiltration of the wall of the aorta and the inferior vena cava with lymphocytes and plasma cells. The walls of both the aorta and the vena cava were markedly attenuated and showed fresh hemorrhage splitting the vessel walls.

Comment

The classic signs of an arteriovenous fistula with right heart failure—widened pulse pressure, peripheral edema, venous distention, enlarged liver—were not apparent in this case due to the rapidity of onset and the large diameter of the fistula. The to-and-fro murmur over the aneurysm and lumbar region was the only objective finding, and its significance was not recognized at the time. Holman[4] has stated that it is an experimentally observed fact that, when a fistula is established between the aorta and vena cava 1-1.5 cm. in diameter, it is invariably fatal. It would appear that the smaller fistulas and those that develop gradually increase the cardiac return at a rate slow enough to allow initial compensation and, finally, the findings of right heart failure. Large fistulas that develop rapidly, such as is reported here, throw such a large burden on the heart that rapid cardiac failure or cardiac arrest is more likely.

Since the inferior vena cava is so closely applied to the aorta and since it is involved in the nonspecific inflammatory reaction that is so characteristic of arteriosclerotic aneurysms, it is interesting that more complications such as this have not been observed. The usual course is leakage into the retroperitoneal space with secondary rupture into the free peritoneal space. Rupture into the duodenum and other portions of the intestine is observed less frequently. With the progressively increasing number of aged persons in our population, more arteriosclerotic aneurysms will be encountered; the possibility of a fistula into the inferior vena cava should be considered in those persons who develop intractable right-sided cardiac failure.

Summary

In a patient with spontaneous rupture of an arteriosclerotic abdominal aortic aneurysm into the inferior vena cava, the fistula developed rapidly, was of large diameter, and precipitated cardiac arrest. Patients with smaller fistulas are more likely to develop intractable right heart failure and this should be considered in the differential diagnosis of this condition. Treatment should consist of resection of the aneurysm, replacement with a graft, and closure of the fistula into the inferior vena cava.

4911 Van Nuys Blvd. (Dr. Greenstone).

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DIABETIC NEUROPATHY PRECIPITATED BY DIABETIC CONTROL WITH TOLBUTAMIDE

Max Ellenberg, M.D., New York

Tolbutamide (Orinase), a sulfonylurea derivative, is an orally given hypoglycemic agent which has recently been added to the therapy of diabetes mellitus. The introduction of any new drug into the therapeutic armamentarium necessarily requires careful observation to detect any toxic manifestations. This applies even more to tolbutamide, since, in addition to being a new drug, it is chemically related to the sulfonamides which have many known undesirable side-effects, the site and mode of action are not clearly defined, its use requires a prolonged period of administration, and it is a substitute for insulin, a known nontoxic agent which has been used safely and successfully for the past 25 years. On the other hand, it is equally important not to attribute to a drug undesirable but coincidental clinical phenomena that are inherent in the course of the disease under treatment and, hence, unrelated to any injurious effects of the medicament per se.

To date, tolbutamide seems to have proved its clinical effectiveness and in many situations has facilitated the control of diabetes. So far, there have been remarkably few reactions and virtually none of any serious nature. Observed side-effects include relatively few hematological reactions, dermatological manifestations, gastrointestinal symptoms, and, more rarely, such ill-defined accompaniments as malaise, headache, weakness, and paresthesias.[1] A case of nephrosis during tolbutamide administration has been reported,[2] but its coincidental association has not been ruled out nor have any similar instances been recorded.

No previous reports of neurological complications have appeared in the literature. The following case reports are presented as instances of diabetic neuropathy after the use of tolbutamide to control the diabetes. It is the aim of this paper to indicate that the neuropathy is not a toxic manifestation of the drug but, rather, it has been precipitated or severely

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From the Department of Medicine, Mount Sinai Hospital.

exacerbated after the institution of good control and while the patients' diabetes remained under good control.

Report of Cases

CASE 1.—On her first Mount Sinai Hospital admission, a 47-year-old woman had the chief complaint of pain in the right armpit, right upper part of the chest, and left lower extremity. The patient's diabetes was discovered five years before, when she visited a physician for weight-reducing instruction. At this time she was obese, weighing 230 lb. (104.3 kg.). Since then, she has lost 120 lb. (54.5 kg.)–100 lb. (45.4 kg.) up until six months before the present admission and another 20 lb. (9.1 kg.) since the onset of the present illness. During this five-year period she tested her urine about once a month, always detecting glycosuria but never having it treated. Six months prior to admission, in the course of a medical examination, glycosuria was again noted and hyperglycemia (blood sugar level 288 mg.%) was documented.

In view of the long-standing untreated diabetes and persistent weight loss, specific therapy in the form of tolbutamide was instituted. The patient received 1 Gm. a day. Fourteen days later she experienced the sudden onset of severe burning pain in the right scapular area radiating into the right axilla and the right breast. Two weeks after this, she noted tingling pain and paresthesias beginning in the left buttock which radiated down the lateral aspect of the left lower extremity to the midthigh. The pains were persistent, severe, and always worse at night and were relieved only by large amounts of narcotics, salicylates, and tranquilizers in combination. There was progressive weakness of both lower extremities, of the left more than of the right, with an accompanying sensation of numbness "as though my feet were no longer part of me." In association with these symptoms, the patient, although usually a jovial person, became depressed and developed anorexia. The patient was given 1,000 mcg. of vitamin B_{12} parenterally daily for three months. Because of the persistence of symptoms and their association with the administration of tolbutamide, the drug was withdrawn after four months. Nevertheless, the symptoms continued unabated.

Her history included total hysterectomy at the age of 23 years for fibroid tumors. The family history revealed the presence of diabetes in her mother, father, and two paternal aunts, one of whom had an amputation of an extremity for diabetic gangrene.

Physical examination revealed a middle-aged woman complaining of pain. Weight loss was evident. Examination of the fundi revealed pinpoint hemorrhages and exudates. Heart and lungs were normal; blood pressure was 130/80 mm. Hg; and the liver was palpable one fingerbreadth below the costal margin. Neurological examination revealed slow cautious gait, difficulty in arising from a squatting position, weakness of flexion at the hips and both knees, absent knee jerks and ankle jerks, hyperalgesia over the right upper thoracic segments T-7 to T-10 and on the left between S-1 and S-3, and decreased vibratory sensation over all the toes. The pupils were unequal and irregular and reacted poorly to light.

Laboratory investigation revealed a normal blood cell count, a trace of albumin in the urine, glycosuria of 1 to 4+, blood urea nitrogen level 13 mg.%, cholesterol level 345 mg.%, alkaline phosphatase level 6.8 King-Armstrong units, sedimentation rate 4 mm. per hour; blood Wassermann test result negative, and fasting blood sugar level 230 mg.%. X-ray of the chest and thoracolumbosacral spine showed normal findings. Lumbar puncture revealed clear fluid under normal pressure with normal manometric reading, cell count, and Wassermann and colloidal gold test results; the total protein level was elevated to 90 mg.%.

In view of the uncontrolled diabetes, the patient was started on tolbutamide therapy, 2 Gm. per day. This dosage was soon reduced to 1 Gm. a day and has been maintained uninterruptedly. While she was in the hospital, her symptoms started to abate and have progressively improved.

The symptoms, signs, elevated spinal fluid protein level, and course in this case were entirely compatible with diabetic neuropathy. Although tolbutamide was suspected as being a toxic agent for the radiculoneuropathy, the course was unaffected by withdrawal of the drug and later by reinstitution of the medication. In fact, the improvement started while she was receiving tolbutamide and continued progressively during maintenance of this therapy.

CASE 2.—A 70-year-old woman had been carefully observed for the possible occurrence of diabetes for many years since her mother, each of her five sisters, and both brothers were known diabetics; two of them had died after amputation for diabetic gangrene. One month ago, she developed pruritus vulvae accompanied by mild polyuria and polydipsia but no weight loss. She quickly recognized the potential significance of these symptoms and instituted dietary restrictions but achieved little success. She therefore presented herself for more specific therapy. There were no complaints referable to the extremities, nor were there any sphincter disturbances. Her history included several attacks of cholelithiasis without jaundice.

On examination the pupils were normal, fundi showed no hemorrhages or exudates, heart and lungs were normal, blood pressure was 160/100 mm. Hg, the liver edge was palpable, and the peripheral pulses were palpable. Neurological examination, including tests of all reflexes and sensory modalities, showed entirely normal findings.

Laboratory examination revealed a normal blood cell count, blood urea nitrogen level 19 mg.%, cholesterol level 254 mg.%, blood Wassermann test result negative, electrocardiogram normal except for left axis deviation, fasting blood sugar level 184 mg.%, and urine normal except for a 2+ glycosuria.

The patient was given 2 Gm. of tolbutamide daily and a diet with 150 Gm. of carbohydrate, 80 Gm. of protein, and 80 Gm. of fat. Within one week she showed definite improvement: the fasting blood sugar level fell to 128 mg.% and the pruritus cleared considerably. The dosage of tolbutamide was reduced to 1 Gm. daily given before breakfast. Three weeks after starting treatment with tolbutamide and diet, the patient complained of numbness in the feet, more marked on the left than on the right and increased at night. The fasting blood sugar level at this time was 150 mg.%. Because of aglycosuria, the dosage of tolbutamide was lowered to 0.5 Gm. daily. However, the numbness continued to become increasingly severe. In addition, the patient now stated that her feet felt cold and "lifeless." At this time, the neurological examination revealed absent ankle jerks with depression of the knee jerk. There was stocking distribution of diminished light touch and vibratory sensations in both feet. Further observation of the patient revealed good control of the diabetes on the therapy with one tablet (0.5 Gm.) of tolbutamide daily. Although the drug was never withdrawn, the symptoms began to disappear two months after onset and were completely gone five months after institution of therapy.

The initial course of this patient seems to relate the neuropathy to the tolbutamide. However, the subsequent course, during which the neuropathy cleared despite continued medication, clearly puts this case into the category of neuropathy after institution of good diabetic control.

CASE 3.—A 72-year-old man had developed diabetes 15 years before. His symptoms at that time consisted of polyuria, polydipsia, and weight loss. He was treated with diet and insulin until four years before the present illness, when his physician died. Since then there had been no observation of his diabetic status. Although he continued to take 15 units of protamine zinc insulin daily, there was slow but steady, progressive weight loss of 20 lb. accompanied by polyuria, nocturia, and dryness of the mouth. He finally consulted a physician, who found uncontrolled diabetes and started the patient on tolbutamide therapy. The patient soon began to feel much better; polyuria, nocturia, and dryness of the mouth disappeared and he began to gain weight. However, four weeks after starting to take the drug, he developed a severe headache in the right temporofrontal area which was followed in five days by diplopia and inability to open his right eye.

Examination at this time revealed a complete ophthalmoplegia on the right. In addition, there was neuropathy involving the lower extremities manifested by absent knee jerks, absent ankle jerks, and absent vibratory sensation below the iliac crests. The blood pressure was 190/100 mm. Hg, urine showed 4+ albuminuria, the fundi did not reveal any hemorrhages or exudates, x-ray of the skull showed normal bones without evidence of injury or increased intracranial pressure, and the edrophonium (Tensilon) chloride test showed negative findings. The diabetes remained well controlled on 1.5 Gm. of tolbutamide, and this dosage was continued without interruption. With no other therapy, the oculomotor paralysis started to clear spontaneously in about one month and disappeared entirely over the course of the next three months.

This case illustrates the occurrence of extraocular muscle paralysis shortly after the institution of good diabetic control with tolbutamide and with complete disappearance of the involvement despite the continued use of the drug. The premonitory severe headache corresponding to the distribution of the first portion of the trigeminal nerve, followed by the nerve paralysis, the complete spontaneous resolution, and the absence of any other neurological disease is entirely compatible with the usual picture and course of extraocular nerve paralysis occurring in patients with diabetes.

Comment

The precipitation or exacerbation of diabetic neuropathy after the institution of control of diabetes has been previously recorded.[3] Recently, this sequence of events has been stressed with emphasis on the fact that the control of the diabetes is the factor involved.[4] Regardless of the means of achieving control, similar results have been noted. For example, although originally referred to in the literature as "insulin neuritis," the neuropathy may occur under comparable circumstances after the control of the diabetes by diet alone.[5] The arguments presented to establish this sequence of events with insulin include these statements: 1. The clinical picture, findings, and course were identical with all other forms of diabetic neuropathy. 2. The neurological syndrome cleared even though insulin administration was continued. 3. The same phenomena have been observed with diabetic control by diet.[4]

The same considerations apply to the case reports presented here. The neurological syndrome in each instance conformed to the accepted criteria of diabetic neuropathy, and the course was compatible with known experience. Above all, the manifestations cleared even though the administration of tolbutamide was maintained. In fact, in case 1, the tolbutamide therapy was reintroduced with no untoward effects; if the neuropathy were a toxic manifestation of the drug, then one would have expected this reintroduction to act as a "challenge" dose. Hence, it may be concluded that the tolbutamide is not the noxious agent but merely acts as the medium for control of the diabetes which in turn, in certain instances, leads to neuropathy. In the same vein, one may confidently predict that, with the forthcoming introduction of other orally given hypoglycemic agents, similar instances of neuropathy after control of diabetes will be encountered.

The etiology and mode of onset of diabetic neuropathy, along with many other factors, remain obscure.[6] It is possible that the relatively sudden change of the homeostasis may produce the equivalent of a stress phenomenon and thus precipitate the neuropathy. This suggestion stems from the observation that other stress phenomena, such as surgery, trauma, and infection, have been known to immediately precede the onset of neuropathy in the diabetic patient.

Summary

In three patients, the onset of diabetic neuropathy followed the institution of control of hyperglycemia and glycosuria with tolbutamide. Although this drug was suspected as being a toxic etiological agent, several factors absolve it of this role: The neuropathy in these circumstances was identical with the recognized forms of diabetic neuropathy, including symptoms, signs, and course; the neurological picture improved and symptoms disappeared despite the continued use of tolbutamide; and similar experiences have been reported with control of diabetes by insulin or dietary restrictions. Thus, tolbutamide is not the noxious agent but acts as the medium for control of the diabetes which, in certain instances, leads to neuropathy.

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SPONTANEOUS REGRESSION OF MALIGNANT DISEASE

GUEST EDITORIAL

Tilden C. Everson, M.D.
and
Warren H. Cole, M.D.

FOR DECADES the reported disappearance or regression of malignant tumors, without significant therapy to explain it, has intrigued the profession, and has given rise to controversy as to whether or not the phenomenon actually exists. Spontaneous regression of cancer may be defined as the partial or complete disappearance of a malignant tumor in the absence of all treatment or in the presence of therapy which is considered inadequate to exert a significant influence on the growth of neoplastic disease. Indeed, spontaneous regression is a somewhat inaccurate term for this phenomenon because any change in the growth pattern of malignant tissue must have a biological explanation.

Efforts to find an explanation of this phenomenon have been thwarted by the fact that, fortunately, only a small fraction of patients with malignant disease go untreated. Thus, spontaneous regression of cancer has been mainly reported in patients in whom the cancer was beyond the scope of cure by the accepted techniques of surgery and/or radiation.

To help find an answer to this phenomenon we have studied the hundreds of cases which have been reported in the world literature since 1900 as examples of spontaneous regression of cancer, and have solicited unpublished reports of cases from our medical and surgical colleagues. The majority of the published cases have been too poorly documented to be considered as valid examples. Most frequently microscopic diagnosis of the malignancy has been lacking.

Of the entire group of cases reported, or made available by our medical friends, we have collected 112 cases which appear to have adequate documentation (including histological diagnosis of the malignancy) to be acceptable as probable examples of spontaneous regression of cancer. This phenomenon was reported most commonly in neuroblastoma (25 cases), choriocarcinoma (14 cases), carcinoma of the kidney (11 cases), malignant melanoma (10 cases), soft-tissue sarcoma (9 cases), and carcinoma of the bladder (7 cases). Spontaneous regression was more rarely reported in the commonly occurring cancers such as carcinoma of the breast (5 cases), carcinoma of the stomach (3 cases), cancer of the colon and rectum (3 cases), and carcinoma of the uterus (3 cases).

The regressions in these collected cases have been divided into two general types: (1) regression of the primary tumor and (2) regression of metastases. In some of the patients with regression of metastases, microscopic confirmation of the metastases is lacking, although in every case microscopic diagnosis of the primary lesion is available. Clinical and x-ray examinations have been the basis of diagnosis of the unconfirmed metastases.

In looking for an explanation of the spontaneous regression of cancer the first consideration is that the original histological diagnosis of cancer may have been incorrect. However, in 67 of the 112 cases tissue slides or photomicrographs have been available for review. Clinical and experimental knowledge indicates the probable importance of endocrine factors in at least some spontaneous regressions of choriocarcinoma, carcinoma of the kidney, malignant melanoma, malignant teratoma, carcinoma of the ovary, and carcinoma of the breast. An impairment of the blood supply appears to be a possible explanation, particularly in the neuroblastomas, since some of these were partially removed at operation and the remaining portion traumatized by the attempt to remove it. Most of the patients with regression of a bladder tumor had had diversion of the urine by transplantation of the ureters. In these cases it would seem that a carcinogenic agent in the urine was necessary for the development and continued growth of the tumor. Fever and/or infection may be implicated as the cause of spontaneous regression in several cases.

Although our study has led us to the conclusion that spontaneous regression of malignant tumors may occur on very rare occasions, we are unable to offer a figure as to its true incidence. This inability to establish a figure of incidence is partly related to the fact that we have no way of knowing how many patients are alive or dead without treatment. We believe the phenomenon is very rare, but it is barely possible that a few of the good results after therapy are related to spontaneous regression.

From the Department of Surgery, University of Illinois College of Medicine, Chicago.

The probability of spontaneous regression occurring in any single case of cancer is so extremely small, however, that any patient would be most foolish to reject orthodox methods of treatment in the hope that his cancer would regress spontaneously.

Evidence of the occurrence of spontaneous regression of cancer supports the concept of biological control of cancer and reinforces the hope that more satisfactory methods of treating cancer than surgery and/or radiation may be found in future years. Also, the occurrence of spontaneous regression of cancer demonstrates the need for caution in the assessment of the value of chemotherapeutic and unorthodox therapeutic measures in isolated "cures" of cancer.

The remote possibility of spontaneous regression of cancer may be of some psychotherapeutic value in offering hope to patients and relatives of patients with "incurable" cancer. Often, indeed, the mere thought that regression might possibly take place changes their attitude from that of complete despair to that of hopeful toleration. The profession should use knowledge of this phenomenon, rare as it is, in an endeavor to comfort the patient and his relatives in the trying days of terminal cancer. With proper precaution the physician can do this without being guilty of offering false hopes.

NATIONAL CANCER INSTITUTE STUDY OF KREBIOZEN

The American Cancer Society statement dated March 9, 1959, which appears in this issue of The Journal, page 1790, urged that the Krebiozen Research Foundation accept the proposal of the National Cancer Institute of the U. S. Public Health Service to test the controversial cancer substance, Krebiozen, in "a manner acceptable to the scientific community." This statement reviews the history of Krebiozen; it clarifies the issues and presents the society's position regarding it.

Since the Krebiozen Research Foundation, its spokesmen, and advocates have "long claimed they have a useful tool against cancer," the American Cancer Society indicated that "it is then their clear duty to thousands of cancer patients to cooperate with the National Cancer Institute or any group of competent, objective scientists in an objective test of the drug." Furthermore, the society indicated that the "delays" which have recently been given so much publicity by the Krebiozen Foundation "are now clearly the responsibility" of that foundation.

The American Medical Association concurs with the American Cancer Society that the prolonged and continued agitation associated with the Krebiozen controversy has a disturbing and unsettling effect on many cancer patients as well as on their relatives and friends, who are bewildered and wonder whether or not the many extraordinary claims made for Krebiozen are actually true.

In 1952 the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association published a lengthy report which did not support the contentions of the promoters of the substance at that time. A Committee on Cancer Diagnosis and Therapy of the National Research Council came to essentially the same conclusions. A committee of six distinguished physicians from several medical schools, headed by Dr. Warren H. Cole, reviewed 500 cases of cancer treated with "Krebiozen" and came up with a number of conclusions, including: "Ignorance of the material interferes with a sound evaluation of its therapeutic effectiveness. . . . no acceptable evidence that any malignant tumor had been cured by Krebiozen. . . . no evidence of prolongation of life. . . . no histological evidence that Krebiozen produced degenerative or regressive changes in tumor cells."

Even though no convincing scientific evidence has been presented during the intervening eight years since the substance was announced, the American Medical Association is currently of the opinion that it is in the public interest that this controversy be terminated. It is in complete agreement with the American Cancer Society that this can be accomplished only through the medium of a thoroughly objective study such as that which the National Cancer Institute has indicated it is prepared to undertake.

Sound research in medicine calls for precise chemical and biological studies, for extensive work on animals, for sustained work in recognized laboratory and clinics, for prior publication in technical journals, for criticism, and for the encouragement of like technical studies elsewhere. These are the proper channels for scientific evaluation of any drug or substance and there is no logical reason why they cannot be followed with Krebiozen.

The American Medical Association, along with the American Cancer Society and, it is believed, with the concurrence of all other scientific organizations expresses the hope that the Krebiozen Research Foundation will recognize the integrity of the National Cancer Institute of the U. S. Public Health Service and proceed to cooperate with this agency that is endeavoring to scientifically evaluate actual and alleged cancer therapy. The American Medical Association believes that in this way the public interest would best be served.

The Krebiozen Research Foundation should desist in its demands for an evaluation of the efficacy of Krebiozen dictated according to its own terms, rules, and procedures which are contrary to the soundly established scientific approaches utilized in the evaluation of substances alleged to be of therapeutic value in malignant disease.

If the representations of the owners and promoters of Krebiozen possess any degree of validity there is nothing to lose and much to gain from such an objective analysis. Failure to accede to such an objective evaluation can be interpreted as an expression of fear or doubt concerning the results of removal of the secrecy which has persistently shrouded Krebiozen through the eight years of its promotion.

ORGANIZATION SECTION

STATEMENT TO SENATE ARMED SERVICES COMMITTEE ON H. R. 2260

March 2, 1959

The Honorable Richard B. Russell, Chairman
Committee on Armed Services
U. S. Senate
Washington 25, D. C.

Dear Chairman Russell:

The purpose of this letter is to submit for the consideration of the Committee on Armed Services the position of the American Medical Association on H. R. 2260, 86th Congress, a bill, which, in part, would extend until July 1, 1963, the induction provisions of the Universal Military Training and Service Act.

With respect to the extension of the special provisions of this Act applicable to medical, dental, or allied specialists, the American Medical Association wishes to reaffirm its position which was outlined in testimony presented in 1957, on the bill which subsequently was enacted as Public Law 85-62, approved June 27, 1957. At that time, the Association testified that, ". . . if the demands for the defense and security of our nation are such that, in the opinion of Congress, it is necessary to have a draft act to maintain the strength of our Armed Forces, then the extension of the present legislation would be one method to insure sufficient physicians for the military services."

The Association also recommended retention of the provisions of the law relating to the national, state and local committees which advise the Selective Service System in regard to the selection of medical, dental and allied specialists required by the services. These advisory committees consider, among other factors, the needs of the civilian population in the communities from which these physicians would be taken. The Association is pleased that this provision is a part of the current law.

In regard to specialist categories, the Association recommends, as it did previously in May, 1957, that the word "other" should be substituted for the word "allied" in this section of the law. This would authorize a selective call for other specialists, such as engineers, physicists, other scientists, et cetera, which might be needed by the military forces. Presently, the law provides only for the selective callup of medical, dental, or "allied" specialists.

The Association believes that physicians should be registered and classified in the same manner as other citizens in the same age group, deferred for educational purposes in the same manner as other registrants and called to active duty or inducted under the same general provisions as other registrants deferred for educational purposes.

It is noted that the pending bill proposes a four year rather than a two year extension of the Universal Military Training and Service Act. We believe the additional two year extension of time should be fully explained and justified to the Committee. We believe that this justification is necessary because scientific and technological advances have resulted in rapidly changing concepts of military manpower requirements. Consequently, there have resulted, directly or indirectly, current and projected reductions in the strength of the Armed Forces. It is conceivable that future manpower requirements may be subject to further downward revisions. A two year extension of the law would permit a timely review of military manpower requirements in light of pertinent changes in the then current military situations. The Association believes that this would be particularly desirable with respect to the callup of medical and allied specialists because of the increasing demands and requirements of the civilian population for the nation's medical and health resources.

As you know from our previous appearances before your Committee, the Association has had a keen and sustained interest in military medicine for many years. Through the Surgeons General of the military services, we have maintained a friendly and close working arrangement in the consideration and advancement of military medical affairs. We feel that the health of the nation requires a careful correlation of military and civilian medicine. In furtherance of this objective, the Association, working with the military services, has attempted to insure improvement in the utilization of medical manpower by the Armed Services and a strengthening of the career incentive program for medical officers.

On behalf of the American Medical Association, I would like to thank you for this opportunity to present our views on H. R. 2260 and to assure your Committee of our willingness to continue our assistance in providing the members of the military services with the finest medical care.

Yours sincerely,
F. J. L. Blasingame, M.D.
Executive Vice-President

STATEMENT OF THE AMERICAN MEDICAL ASSOCIATION ON S. J. RES. 41, 86th CONGRESS

THE INTERNATIONAL HEALTH AND MEDICAL RESEARCH ACT OF 1959
SENATE COMMITTEE ON LABOR AND PUBLIC WELFARE
BY GUNNAR GUNDERSEN, M.D.
FEB. 25, 1959

Mr. Chairman and Members of the Committee:

I am Dr. Gunnar Gundersen, a practicing physician from LaCrosse, Wisconsin. I currently am serving as the President of the American Medical Association, on whose behalf this statement is presented.

In addition to my position with the A. M. A., I am a member of the Council of the World Medical Association, an organization of 53 national medical associations comprising a membership of more than a half million physicians.

With your permission, Mr. Chairman, I should like to discuss briefly the interest and activities of the American Medical Association in connection with international health, medical care and medical education, and the philosophy and position of the A. M. A. with respect to the subject resolution which would establish a National Advisory Council for International Medical Research.

For many years the American Medical Association has played an active and far-reaching role in the international health field, because of its belief that physicians on every continent are dedicated to the assistance of all people regardless of race, color, creed, or social class in attaining the highest possible level of health.

Here briefly are a few of the ways in which the A. M. A. has acted specifically upon this belief:

1. The Association helped to organize and support the World Medical Association in 1948. We also approved and encouraged a United States Committee to aid the World Medical Association financially. This committee has provided, and is furnishing, funds to help finance the W. M. A. Secretariat, the publication of the *World Medical Journal,* and specific scientific investigations.

2. An A. M. A. representative has served with the U. S. delegation to the Assembly of the World Health Organization, a subsidiary of the United Nations representing governments in the field of medicine.

3. THE JOURNAL of the American Medical Association is promoted in foreign countries, and now serves as an "up-to-the-minute" medical textbook for approximately 10,000 subscribers overseas. It can be found in every recognized medical library in the world.

4. Likewise, our nine specialty journals reach thousands of physicians outside the United States, providing them with the latest medical information on subjects relating to their specialties.

5. The A. M. A. has established, developed, and maintained the valuable "Standard Nomenclature of Disease and Operations," the only international publication of its type.

6. The A. M. A. library staff compiles the "Quarterly Cumulative Index Medicus," a publication providing pertinent information on medical periodicals, literature, and books. Currently there are more than 1,300 foreign subscribers.

7. Other A. M. A. publications which have wide appeal among physicians abroad include "New and Non-Official Remedies" and "Useful Drugs." These publications provide physicians with information on the actions, uses, limitations, and dosages of new drugs.

8. A. M. A. medical films are loaned to medical societies all over the world. In the past 10 years the A. M. A. has received approximately 775 unsolicited requests from 70 countries for medical films. While it was impossible to fill all the requests, hundreds of films have been provided on a loan basis.

In addition, the A. M. A. has cooperated with many national medical societies in arranging film programs. This year a special film program has been prepared for the Japan Medical Society.

9. The A. M. A. has been vitally interested in the training, in American hospitals, of physicians educated abroad and is a participating member of an evaluation service for foreign medical graduates. In 1957-1958 a total of 7,622 physicians from 90 countries were trained in American hospitals as interns or residents. (Open Doors, 1958, prepared by Institute of International Education.)

10. This year the American Medical Association, along with the Association of American Medical Colleges, will play host to the Second World Conference on Medical Education in Chicago (Aug. 30-Sept. 4). Our Association again is giving its wholehearted cooperation to this conference which is expected to draw more than 1,500 persons from all parts of the world.

I am sure all of you are familiar with the dramatic television production, "MD International," sponsored by Smith, Kline & French Laboratories and the American Medical Association. The film was inspired by President Eisenhower's People to People speech, in which he said that one of the best roads to international understanding was through constructive personal contact among individuals of all nations.

"MD International" was premiered at the 1957 Clinical Session of the American Medical Association in Philadelphia. In introducing it, Dr. David B. Allman, who was then President of the Association, said:

"MD International is a warm and inspiring account of the activities of American doctors who chose to practice in the far corners of the world.

These physicians, and many like them, act as our unofficial medical diplomats. Not only do they carry modern medicine to people in remote areas but they also—through their daily lives and through dedication to their patients—help spread good will and understanding.

"The contribution of these doctors of medicine is a great steppingstone on the path to peace."

I have mentioned some of the ways in which the American Medical Association is working, with others around the world, to promote better health, medical care, medical facilities, and medical education.

Our Association feels that medicine has no geographical boundaries, for it truly is an international science for the benefit of everyone. Furthermore, we believe that only through coordinated effort can physicians throughout the world bring to their people the maximal health benefits that modern medicine can provide.

Today more than ever before medical men all over the world are interdependent. Consequently, physicians in America are interested not only in exporting new developments in the art and science of medicine but also we are equally anxious to import new techniques and discoveries by our colleagues in other countries. World-wide progress in medicine can continue in the future only through the free exchange of ideas between medical scientists in all countries.

Last June at the presidential inaugural ceremony of the American Medical Association I titled my address "Physicians to the World." Allow me to quote a few of the concluding lines from that address:

"In medical science there are no secrets, no iron curtains, no cold war. To physicians everywhere, atomic energy means a new way of fighting disease, not a new way of conquering the world. Medicine exists to save life, not destroy it."

Since medicine speaks a common language around the world we can combat physical and mental suffering with more medical knowledge and research. Obviously, there are enormous potentials for health and good living which are still unrealized both in the United States and in all other countries. In addition, there is a growing recognition that medicine, with its resources and influence fully mobilized, can perhaps do more for world peace than the billions of dollars being poured into armaments. There is a mounting conviction that the time has come when medical statesmanship must be used to augment the methods of political diplomacy.

I believe that Senate Joint Resolution 41, 86th Congress, will provide an important way in which the United States can contribute to the health and well-being of our own citizenry and of all the peoples of the world.

We in medicine have long recognized that native intuition and the ability to apply scientific methods of research are gifts which are not confined to people in only a few nations of the world. Men and women of science in all countries can contribute substantially to the expanding horizons of medical knowledge.

The establishment of the National Advisory Council for International Medical Research and the National Institute for International Medical Research can provide a vital vehicle for implementing and assembling our existing and potential forces of medical science.

After careful study of Senate Joint Resolution 41, I have a few other points that this committee may want to consider:

1. I believe that the World Medical Association is another of the already existing, tested means for international cooperation in matters relating to health. Therefore, it should be included along with the World Health Organization, the Pan American Sanitary Bureau, and the United Nations International Children's Fund, as international groups to cooperate with.

2. I agree basically with the manner in which the Council is to be appointed—"by the Secretary without regard to civil service laws." However, it would be my suggestion that the Secretary of the Department of Health, Education, and Welfare rely heavily on the surgeon general of the Public Health Service in making the appointments because of the professional character of the Council.

3. Naturally due care must be taken in supporting researchers in foreign countries because of the possible salary differential. While the financial grants to foreign researchers must be adequate—perhaps even attractive—the secretary and his advisers must see that the program does not adversely affect medical care and scientific research in foreign countries.

4. Generally, the Senate Joint Resolution deals with research, investigations, and experiments by individuals, universities, hospitals, laboratories, or other public agencies or institutions. However, there is a reference to grants for the improvement or alteration of facilities needed for medical research and research training. I believe that the

program should be one of research and not a research construction program. Perhaps it would aid and guide the secretary, the surgeon general, and the council if some general qualifications or limitations on grants for the improvement or alteration of facilities were added.

5. Finally, I believe that the greatest care should be exercised in setting up the research grants and research programs. Because of the vast amount of research being conducted today, all proposed projects must be scrutinized carefully.

Last December in my report to the House of Delegates of the American Medical Association, I stated that medicine should offer leadership and imagination on the international scene. At that time proposals for an International Medical Year were being made. In support of such a project I said that the American Medical Association should offer maximum help and leadership as a contribution to world understanding.

In furtherance of this belief, the American Medical Association offers its full support and assistance in the establishment of the National Advisory Council for International Medical Research and the National Institute for International Medical Research, proposed by S. J. Res. 41. We believe that the promotion of international health through research is one of our best means of promoting international cooperation and understanding. Whatever we do to promote good health also will promote peace in the world.

Thank you, Mr. Chairman and members of the committee, for giving me this opportunity to testify here today.

COUNCIL ON MEDICAL SERVICE

CHRONIC ILLNESS INFORMATION CENTERS

In most cities a wide variety of services and facilities are available for long-term patient care. These may range from a chronic disease hospital or an organized home-care program to nursing homes or visiting nurse and homemaker services. Whatever their function or sponsorship, they are too frequently either unknown to or overlooked by physicians having patients with illnesses that do not require general hospital care.

A comparatively recent approach to the better utilization of such services and facilities has been the establishment of what are being variously termed "central services for the chronically ill," "chronic illness information centers," or the like. These agencies provide information and referral services to physicians or to patients seeking the proper facility, conduct fact-finding studies on needs and resources for care, stimulate and coordinate planning, and, in general, serve as community clearing-houses on chronic illness planning and activity. The first such service was established in Chicago in 1944. Four others have been organized along similar lines at later dates in San Francisco, Milwaukee, Cleveland, and Essex County, N. J.

Although these agencies differ in the emphasis placed on various facets of their operation, all are organized to a greater or lesser degree around the following general functions: (1) to collect and maintain current information on all available community facilities and agencies offering service to the chronically ill or aged and to provide referral services to individual patients or other persons seeking the appropriate service; (2) to provide consultation and guidance to the operators of nursing homes, homes for the aged, and other long-term facilities in regard to standards of care, operating methods, and costs; (3) to conduct or participate in fact-finding research into the prevalence of long-term illness or disability in the community, the important unmet needs for care, and the additional facilities and services necessary; and (4) to initiate, stimulate, and coordinate community planning to meet these needs, through contacts and conferences with appropriate groups and individuals and through public education, both professional and lay.

The Council on Medical Service has undertaken an expanded program of research, education, and implementation in the various problem areas of aging and long-term illness. Because of the important role such information and referral centers play in coordinating care for these two groups, it was decided to gather information on their organization and operation, the types and needs of persons they serve, the special programs and projects undertaken, and the major problems encountered in serving the aged and chronically ill.

Reports on the chronic illness centers in Chicago and Milwaukee follow. Reports on the other three centers will appear in subsequent issues of THE JOURNAL. It is believed that the data obtained will be of interest to physicians, medical societies, and other groups and individuals who are either involved in the care of these types of patients or concerned with the over-all problems of aging and long-term illness.

CENTRAL SERVICE FOR THE CHRONICALLY ILL OF THE INSTITUTE OF MEDICINE OF CHICAGO

The Central Service for the Chronically Ill of the Institute of Medicine of Chicago began operation in January, 1944, with the financial sponsorship of the Community Fund. Its inception had been preceded by more than 10 years of increasing concern and tentative planning for the growing number of chronically ill in Chicago, on the part of various committees of the Welfare Council, the Institute of Medicine, and other medical, public health and welfare agencies. In the fall of 1942, plans were crystallized when the Welfare Council Committee on Chronic and Convalescent Care recommended that a special agency be established to devote full-time attention to the needs of the chronically ill and the community services necessary to meet these needs. It was intended that the agency would serve as a central point for assembling comprehensive and current data on facilities for the chronically ill in Chicago and on the improvements and additional facilities needed, would concentrate the interest of medical and welfare groups and the general public on these unmet needs, and would formulate specific proposals for improvement of care. It would also provide information on the best services available to patients or other persons seeking care.

In the belief that the work should be under medical auspices, the welfare council had approached the Institute of Medicine during the planning stages with a suggestion that the institute sponsor the project and had added representatives of the institute to the planning committee. Funds for the work became available before final arrangements for sponsorship had been completed, and, to avoid delay, the project was established under the auspices of the welfare council, with institute representation on the governing committee. It operated in this way for the first four months of its existence. On May 1, 1944, it was formally transferred to sponsorship of the Institute of Medicine with the same governing committee, including representatives of the welfare council, and with the same staff and program. A representative of the welfare council continues to serve on the governing board of the Central Service for the Chronically Ill, and, in this and other ways, efforts are made to coordinate the work of the two organizations.

Early in the work of the central service the purposes and program were broadened to include activities directed toward prevention and control of long term illness, as well as toward the improvement of care. These revised purposes, which have directed the central service's activity to the present, are (1) the determining of the important problems of chronic illness in the community through fact-finding studies and accumulation of information from other sources on the number of chronically ill persons, the nature of their disabilities, the services required to meet their needs, the kinds of agencies and institutions best able to provide the necessary services, the part each should play in the total community program, and the ways in which the various personnel, agencies, and institutions should be integrated with each other in providing service; (2) the development of a comprehensive plan outlining the additional services and facilities required in the community and promotion of the development of these facilities through education, consultation with persons and organizations planning new facilities, and other methods; (3) the promotion of the most efficient use of existing services by providing information, counseling, and referral to patients and their families, physicians, health and social agencies, and others seeking suitable facilities for care; (4) the furthering of the effective programs for the prevention and control of long-term illness by encouraging additional effort in this field and by coordinating the facilities and services for care with those whose primary activities are related to prevention; and (5) the fostering of good standards of care and rehabilitation for the chronically ill and disabled at home and in all types of institutions by developing and making available to the personnel and institutions involved specific descriptive and standard-setting material on the quantity, quality, and reasonable costs of services and supplies necessary for adequate care, and by providing consultation in problems of management and administration to these institutions and facilities.

Although the information and counseling service has been operated continuously since the central service was established, a major part of the organization's work up until 1954 revolved around the collection of community-wide data on the needs of the chronically ill, the formulation of standards, and the development and promotion of a community plan to meet the needs. By 1954, the major community problems of chronic illness had been identified and clarified. Information had been collected on the types and extent of additional services and facilities needed, the advantages and disadvantages of various methods of organizing these services, costs, and possibilities for financing; the comprehensive community plan had been developed. This brought to a close the temporary purposes for which the center had been established.

The need continued, however, for referral and counseling services to individual patients and for guidance and consultation to facilities caring for these patients, particularly private nursing homes. In response to considerable community pressure, and with financial help from the Chicago Medical Society, Community Fund, Chicago Community Trust, Illinois Division of the American Cancer Society, Chicago Heart Association, and some private foundations, the central service was established on a permanent basis in the Institute of Medicine to continue these two functions. It has been operating on this basis up to the present.

Organization and Operation

The central service now occupies an office in the John Crerar Library Building adjacent to the general offices of the Institute of Medicine in downtown Chicago. Organized as a separate corporation, it operates under the jurisdiction of the Institute of Medicine's Committee on Chronic Illness, which acts as the board of directors. This committee includes eight physicians, an administrative nurse, an executive of the welfare council, two lawyers, and four other lay persons.

The agency began operation with a staff of five: a director, a consultant on standards who was a home economist familiar with the development of quality-quantity-cost standards, a nurse and a medical social worker designated as consultants on resources, and an office secretary. With the termination of the special fact-finding phase of the agency's work, the position of consultant on standards was discontinued. An additional typist has since been added, leaving a present active staff of five.

The director of the central service is a registered nurse, with a bachelor's degree. Her duties, in addition to administrative supervision of staff, include reporting to the board on all agency operations and activities and implementing all decisions of this group, formulating new policies and programs, employment of personnel, expenditures of funds, and representing the service to the community.

The two consultants on resources are responsible for the collection and maintenance of information on the available nursing homes, institutions, agencies, and other facilities in the community and for day-to-day counseling with patients and other persons seeking suitable facilities for care. Information is collected and kept up to date through visits, telephone calls, summarizing of reports from agencies, institutions, and patients, and other methods. Much of the work toward improving quality of care is carried on during visits to the homes and institutions, through the provision of consultant service to operators of the facilities, and through the distribution of printed material.

The secretary and a typist handle the major part of clerical-administrative detail inherent in the agency's operation. Their duties include maintaining administrative files of the agency, preparing financial and statistical reports and records, handling staff schedules and payrolls, purchasing of supplies as authorized by the director, and performing stenographic work for the professional staff.

Request for service forms are kept for each patient or other person contacting the central service, giving diagnosis, degree of disability, services requested and needed, action taken, and other pertinent information. The service also maintains detailed individual records on agencies, homes and institutions, sources of financial assistance, and all other resources for long-term care or service in the community, and it has abbreviated this information in a desk card file for quick reference. Finally, the service maintains over-all statistical information on the relationship of needs and resources for care in Chicago. This includes full information about resources for care of patients in their homes and a yearly register of all nursing and old-age homes, hospitals, rehabilitation centers, and other institutional facilities serving long-term patients, giving bed capacity and type of ownership or auspices.

Services to Patients

In line with the central service's policy to act purely as an information and counseling center, rather than as a case-work agency, persons requesting service are accepted without any prior investigative procedures. For this same reason, and because of the expense involved, the service does not attempt any organized follow-up of patients to see whether a satisfactory solution or placement has been completed.

The service has not attempted any community-wide publicity campaign directed toward patients or other agencies. The annual reports of the central service are reprinted in the Proceedings of the Institute of Medicine, and there has been an occasional article or editorial in this publication. Notices of the availability of the service are published from time to time in the Bulletin of the Chicago Medical Society, and descriptive listings are carried in the Welfare Council's Social Service Directory and the classified telephone directory.

There have been a number of informational mailings about the service to physicians in Chicago and Cook County, and a letter and leaflet recently were sent to all physicians in the area, all clergymen, and a selected list of lawyers, trust officiers, and personnel directors in various business and industrial establishments. Finally, there have been sporadic newspaper articles and radio announcements concerning the availability of the service. Current thinking is that more publicity specifically directed toward the service's informational and counseling functions would be helpful.

During the calendar year 1958, a total of 2,892 patients or other persons sought information or counseling at the service center. Of these requests for service, 433 were recall cases, or patients who had previously contacted the center and 314 were requests for service not related to an individual patient. Table 1 shows the number of requests during 1956, 1957, and 1958, divided by new and recall cases, and other requests not concerned with a specific patient.

A special tally of a randomly selected 100 patients served during December, 1957, shows that 83% of these were over 60 years of age. Three-fifths, or 60% of this group, were women, a proportion which has held relatively constant over the years of operation. Of the cases on which the data were available, 27% of the patients were married and 73% were single, widowed, separated, or divorced; 26% were in hospitals at the time of contact, and an additional 14% were in nursing homes, boarding homes, and other institutions; 14% were living at home with husband or wife, 27% with other relatives or friends, and 19% alone. The proportions of ambulant, semiambulant and bedridden patients referred to the service have been relatively constant since its inception, as have been the number of patients able and unable to pay full costs of care.

TABLE 1.—*Persons Served in 1956, 1957, and 1958*

Year	Patients, No.		Other No.‡
	New*	Recall†	
1956	1,509	226	227
1957	1,721	334	225
1958	2,145	433	314

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* Patients known to center for first time.

† Patients who have received previous service from center.

‡ Requests for service not related to specific patient.

Table 2 gives a breakdown of these 100 newly referred cases by age, degree of disability, financial status, source of referral to the service, and other characteristics.

Needs of Patients

During September and October, 1958, nearly 65% of patients contacting the central service for the first time requested nursing home or other institutional care. The next most frequent requests were for some type of housekeeper-attendant service and for general counseling and help in planning a patient's care. Other requests were for information on some specific facility, home nursing care, or rehabilitation services. Table 3 shows the nature of requests for service among 638 calls received by the central service during September and October, divided by new and recall cases. Also included are calls received from nursing home operators on management problems, from persons planning to establish such facilities, and from individuals and organizations seeking general information on needs and resources.

Some 60 to 65% of all patients requesting service are given help in finding homes and institutions providing long-term care. Another 10 to 12% of patients are given information or counseling on home-care services or resources for financial assistance. Five to eight per cent of patients are referred to social case work agencies. Other referrals are to rehabilitation facilities and similar community services. For a small number, further medical or psychiatric evaluation is recommended before attempting a plan for care.

Problems and Developments

The important unmet needs and problems of Chicago's chronically ill, as evidenced by requests to the central service and by its extensive fact-finding work in the community, seem to revolve around a need for substantial improvements in financing of services; a shortage of good inpatient facilities for long-term care; a need for broadening the range of services offered, especially rehabilitation services within the various long-term institutions; some deficiency in the services available to help patients and their families at home; and a need for closer coordination of the activities of the many different organizations now becoming involved in the planning and development of community services in the field of chronic illness.

At present, in Chicago, there are about 16,000 beds for long-term care—in special hospitals for treatment and rehabilitation of the chronically ill; in voluntary, public, and private nursing-care facilities; and in infirmary sections of homes for the aged. Although this represents an encouraging growth from the some 10,000 beds available at the time of the central service's inception, and is not far short of the total number needed, at least 6,000 of these presently available beds are of such poor quality and offer so little possibility of substantial improvement that they should be replaced by new facilities. Most of these 6,000 substandard beds are

TABLE 2.—*Characteristics of One Hundred Patients Newly Referred to Center, December, 1957*

	Patients, No.
Sex	
Male	40
Female	59
Not recorded	1
Age	
<20	2
21-40	2
41-60	10
>60	83
Not recorded	3
Marital status	
Married	23
Single	15
Widowed, divorced, or separated	46
Not recorded	16
Living arrangements	
Alone	17
With spouse	13
With relatives or friends	25
Boarding or nursing home	12
Hospital	24
Other institutions	1
Not recorded	8

	Patients, No.
Degree of disability	
Ambulatory (includes senile)	45
Semiambulatory	26
Bedfast	28
Not recorded	1
Method of contacting center	
Phone	93
Letter	3
In person	4
Main source of income or support of referred persons*	
Spouse	6
Other relatives and/or friends	24
Old Age Assistance	9
Old Age Assistance, relatives, Old Age & Survivors Insurance, etc.	5
Other public welfare	2
Pensions	16
OASI, savings, relatives	8
Business, employment, rentals	1
Savings only	2
Capital assets, convertible property	3
Disability and employment insurance	...
No income	1
Not recorded (unknown)	5
Private funds (exact source not specified)	18

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* Figures are weighted toward self-supporting persons, as arrangements for care of financially dependent usually are made by welfare agencies.

in small proprietary nursing homes in the city, and the central service feels that this is a reflection of two primary factors. One of these is the fact that many of the operators of these facilities have not had the experience or training necessary to provide good care economically and efficiently. Until recently there have been no institutes, training centers, or other educational resources from which these operators could obtain guidance in organizing and operating a nursing home, or even any books or journals devoted to this subject. There has been a definite need, first, for a specific definition of what good care consists of, and what is required to provide it in terms of organization and ownership of nursing home facilities, relationships between these facilities and other inpatient care institutions, physical plant and equipment, numbers and training of personnel required, and costs; and, second, for educational channels through which this information can be made available to the owners and operators of the facilities.

A major part of the central service's work has been directed toward these needs. A 400-page book giving practical guidance for persons planning to establish new homes and institutions has been published by the service, and a companion volume on organization, management, and budgeting procedures is forthcoming. Hospital organizations and journals are publishing material of this type with increasing frequency. A number of short training courses covering patient care, personnel, management, budget, and other such areas have been set up for nursing home owners and operators, and efforts along this line are increasing. The second important factor in the inadequacy of many proprietary nursing homes has been the lack of sufficient funds to provide good care, particularly for public assistance recipients.

The central service continues to urge and work for more realistic standards of payment for public assistance recipients, through its contact with other agencies and individuals in the community, talks and programs before interested organizations, and cooperating with the Health Division of the Welfare Council in efforts to improve the payment standards now in use by the Illinois Public Aid Commission.

Services to the Community

From its inception in 1944 up until 1955, a major part of the central service's work was taken up with various special studies into the nature, prevalence, and problems of chronic illness in the Chicago area. In addition to the broad, day-to-day collection of information on the number, types, and needs of chronically ill, and the community services required to meet these needs, the service has completed the following specialized studies: (1) terminal care for cancer patients—a study of the facilities available and needed in Chicago for care of this group, specially financed by the American Cancer Society; (2) a specially financed study of the services available and needed for home care; (3) the need for institutional facilities for the long-term care of children; (4) the need for special institutional facilities for young adults; (5) an analysis of personnel and services required in different types of homes and institutions for long-term care; and (6) costs of care in long-term institutional facilities, compared with the costs of home services for the chronically ill.

By the end of 1954, the central service had identified and clarified the major problems and unmet needs of the chronically ill in Chicago and had assembled information on the services needed and extent of the need, types and numbers of agencies and institutions required, the pros and cons of various forms of organization of services, probable costs, and the possibilities for financing. The central service has developed and is planning to publish a model plan for a coordinated community-wide program in Chicago directed toward all aspects of the chronic illness problem—early diagnosis and prevention; care and rehabilitation of the long-term patient at home, in hospitals, nursing and old-age homes, and other institutions; coordination of community facilities and services; fund-raising and financing of care; maintenance of statistical information on needs as related to facilities available; and the basic community and professional services needed in research, professional, and public education, and licensing and standard setting for institutions and personnel.

Table 3.—*Nature of Requests for Service Among 638 Calls Received During September and October, 1958*

Type of Request	Percentage of Total Cases		
	New Cases	Recalls	Total
Nursing home, boarding home, institution	64.2	60.3	63.7
Nursing home and financial assistance	2.7	1.4	2.5
Housekeeper, attendant, etc.	7.6	1.3	6.9
Nursing care in patient's home	1.8	...	1.6
Information re facilities and resources			
Sheltered or home employment	0.2	1.4	0.3
Financial assistance	1.6	1.3	1.6
Rehabilitation services	1.6	...	1.4
Wheel chairs, hospital beds, etc.	0.3	...	0.3
Medical and dental care, free or cheaper medicines	0.4	...	0.3
Transportation to clinics	0.2	...	0.2
Recreation and companionship plus medical and dental care	0.2	...	0.2
Day care	...	...	...
Restaurants serving special diets	...	...	...
Miscellaneous procedures, legal advice, camp, etc.	0.3	...	0.3
Information regarding a specific facility	4.1	5.5	4.2
Help in formulating specific plan for care of patient, information about various types of facilities	6.2	5.5	6.1
Information on costs of care	0.3	...	0.3
Consultation to nursing home managers on management problems	1.6	...	1.4
Consultation to persons planning establishment of new facilities	2.3	...	2.1
Consultation to persons and organizations seeking information about care of chronically ill (including statistical data, information on costs of care, and standards)	4.4	...	3.9
Additional information only	...	23.3	2.7
Total	100	100	100

Other material published or about to be published by the central service includes a 25-page pamphlet summarizing methods for surveying community needs and resources for long-term care; a 55-page booklet on the role of the nurse in caring for the chronically ill; a monograph on community services for rehabilitation; a monograph on licensing and standard-setting for long-term care institutions; a casework manual for welfare agencies to assist them in arranging care for the chronically ill patient; and a monograph on home-care services.

Finally, the professional staff of the service continues on a day-to-day basis to counsel with the operators of institutions providing long-term care, particularly privately owned nursing homes, in efforts to develop and maintain good standards of care, and to maintain and make available to the community centralized information about the needs and resources for care of the chronically ill in the Chicago area.

CENTRAL AGENCY FOR THE CHRONICALLY ILL OF MILWAUKEE

The Central Agency for Chronically Ill, of Milwaukee, was established in February, 1948, as the result of a two-year study into the problems and unmet needs of chronically ill persons in Milwaukee County. This study, which was financed by the Women's Club of Wisconsin and conducted by a special study committee of physicians and other citizens appointed by the Community Welfare Council of Milwaukee County, showed a need for some type of central clearing house to collect information on the facilities providing long-term care and the additional facilities and services needed in the county. The study committee was then charged with developing, in cooperation with other agencies, a central information-gathering and educational service for the chronically ill.

The central agency was supported through its first years by a grant of $10,000 from a service club and presently by the Community Chest, of which it is a participating agency. Its objectives are (1) to gather and maintain current information on nursing homes, homes for the aged, and other facilities providing service for the long-term patient and to assist with placements in these facilities; (2) to stimulate through community education the setting aside of additional hospital beds for long-term illness, the expansion of good nursing home facilities, the extension of bedside nursing care in private homes, and the development of additional facilities for recreation and rehabilitation; and (3) to stimulate further study of degenerative diseases from all aspects.

Organization and Operation

The central agency occupies a small office in the downtown Milwaukee area. The original staff consisted of the executive director and an office secretary. A professional staff worker was added as operations progressed. The central agency functions under the supervision of a 21-man board of directors, representing the fields of medicine, industry, finance, law, the clergy, public relations, and service groups. This board, which meets once monthly, is responsible for over-all policies of the agency and for approving budget expenditures and any changes or additions in the agency's program. The agency is organized as a corporation, with an unlimited number of members who are elected for five-year terms. These members represent various fields and professions in the community, participate in special program meetings several times a year, and serve as a reservoir from which to draw new members for the board of directors.

The executive director of the agency is a registered nurse, with a masters degree in public health. Her duties, in addition to over-all administrative supervision of the agency and preparation of the budget, include formulating new programs and policies for the agency and submitting them to the board of directors and the Community Welfare Council, interpretation of agency policies and programs to the community, developing educational programs and institutes directed toward the general public and various professional groups, securing data and preparing reports on the individual and community problems of long-term illness, and continuous liaison with other community social and health agencies in order to foster a coordinated approach to problems of the chronically ill.

The professional staff worker is a registered nurse with a degree in public health nursing. Under supervision of the executive director, she is responsible for counseling and referral of patients seeking nursing homes and other facilities for care, for visiting and evaluating all nursing, old-age, and foster homes within a 50-mile radius of Milwaukee, for keeping a running file on these facilities, and for consulting with persons planning new nursing homes and other such facilities in regard to standards of care. Her duties also include meeting regularly with state and local organizations of nursing home operators and assisting these operators with problems related to management efficiency, nursing care, and costs.

The office secretary handles most clerical-administrative detail in the agency's operation, including typing, maintaining files and records, and serving as receptionist and telephone operator. Monthly narrative, statistical, and financial reports on the agency's operation, in addition to an annual report, are prepared jointly by the director and the staff worker and distributed to the board and all corporation members. Other records and files maintained in the office include request-for-service forms for all patients or other persons seeking information—these include diagnoses and the name of the physician in charge for all patients—a complete nursing home evaluation report on all facilities visited by the staff worker and a summary of these evaluation reports in a desk card file. The agency also maintains a reference library of books and other educational material.

Services to Patients

About one-fourth of the time of the professional staff is taken up with counseling and referral of patients to nursing homes or other institutions and services for the chronically ill. The central agency has not attempted any intensive publicity toward this facet of its operation. Articles noting the availability of the counseling service have been published from time to time in the local newspapers, and the agency has published brochures or pamphlets directed toward persons seeking information on the services available in Milwaukee. Patients seeking information or placement counseling are accepted for service without any prior investigative or casework procedures. The agency has at times had sample clearances with the Social Service Exchange in Milwaukee but decided against making it a routine practice. The agency does not attempt any organized follow-up of patients to see whether the referral or placement made in individual cases has been completely satisfactory.

TABLE 1.—*Characteristics of Patients Newly Referred to Center in 1957*

	Patients, No.
Sex	
Male	199
Female	314
Age	
<20	2
21-40	17
41-60	47
>60	447
Marital status	
Married	72
Single	91
Widowed	305
Divorced or separated	2
Not recorded	43
Living arrangements	
Alone	126
With spouse	64
With relatives or friends	115
Boarding or nursing home	20
Hospital	126
Other institution	48
Not recorded	14

	Patients, No.
Degree of disability	
Ambulatory	146
Semiambulatory	241
Bedfast	126
Method of contacting center*	
Phone	437
Letter	27
In person	99
Main source of income or support of persons referred	
Spouse	24
OAA plus relatives, OASI, etc.	62
Pensions (retirement, veterans, etc.)	47
OASI plus savings, relatives, etc.	39
Income from business, employment, or rentals	338
Savings only	
Capital assets, convertible property	
Not recorded (source unknown)	3

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* *Includes more than one type of contact by some patients.*

The number of patients and other persons seeking help at the agency has increased slowly but steadily since its inception in 1948. In the fiscal year 1954-1955, 619 new patients or other persons contacted the agency for service; in 1955-1956, 688, and in 1956-1957, 693 new patients were served by the agency. At present patients are referred to the agency by their families, themselves, the Visiting Nurse Association, hospitals in Milwaukee, physicians, lawyers and courts, and friends, in about that order of frequency.

Of the 513 individual patients referred to the agency during the calendar year 1957, over 85% were 60 years of age or older. This age percentage has held relatively constant over the years of operation, with an average patient age near 75. Over three-fifths of patients referred to the center were women, a proportion which has also held constant. About 77% of the patients were widowed or single, 25% lived alone, and 22% lived with relatives. An increasing percentage of bedfast or incapacitated patients have sought help at the agency in recent years. The percentage of senile or mentally disoriented patients referred to the agency has also risen. Table 1 shows the characteristics of individual patients referred to the agency during the calendar year 1957 by age, degree of disability, living arrangements, financial status, and other factors.

Needs of Patients

In the period from October, 1957, through September, 1958, requests for 24-hour nursing, boarding, or other institutional care accounted for a little over 36% of all needs for service among newly referred patients or other persons. The next most frequent requests were for counseling or educational material. Other frequent requests among new contacts were for information on establishing a new facility for care and for information on sheltered or home employment and custodial day care. Table 2 shows the nature of requests for service received during this period, divided according to new and recall patients. Not included in this tabulation are some 259 calls received from nursing home operators during this period, reporting vacancies or the filling of vacancies in their facilities.

The community facilities or services to which patients are most frequently referred have been nursing and old-age homes, the Welfare Department, Visiting Nurse Association, the Family Service Agency, and the local Old-Age and Survivors Insurance (OASI) Bureau.

Problems and Developments

As a result of its referral and fact-finding work with patients and other individuals and agencies in the community, the central agency has been able to pinpoint some of the more pressing problems in meeting the needs of Milwaukee County's chronically ill. There is an urgent need at present for some type of visiting homemaker or housekeeper service which could be made available to the considerable number of chronically ill or infirm patients living at home. Such a service has been approved by the Visiting Nurse Association, but its inception has been delayed by a difficulty in recruiting housekeepers. The central agency is also planning to inaugurate, on a demonstration basis, an organized home-care program similar to those operating in other communities. This project is presently awaiting the approval of the Milwaukee Medical Society.

Another major problem is the lack of suitable facilities for care of the "in-between" type of senile patient, who is too much of a supervisory problem for the average nursing home operator but does not need or belong in a mental institution. Progress on this problem has been nil to date. There is also a lack of suitable nursing care facilities for persons in the middle and higher income group who desire and are able to pay for a private room and bath. The central agency, in its consultation work with nursing home operators, has stimulated those persons planning new or improved facilities to include more such private and semiprivate accommodations in their planning.

Finally, the agency feels that there is a definite need for additional organized inpatient rehabilitation services. Milwaukee has adequate rehabilitation services at the outpatient level, but more inpatient facilities than those presently provided by the general hospitals of the city are needed.

Services to the Community

More than 40% of the working time of the director and staff worker is taken up with activities of a community-wide nature—classes, talks and other educational projects, visits to nursing homes and counseling with their operators, and assistance to nursing home organizations, both state and regional. The central agency has sponsored, organized or participated in a number of annual workshops for nursing home operators. These workshops have utilized the educational resources of a number of state and local agencies and organizations and have covered such areas as nursing service, nutrition, rehabilitation, administration, budgetary and management problems, enlistment and training of nursing home personnel, and broad trends in the nursing home field. The first such workshop was given by the agency in Milwaukee in 1951, with the help of the newly formed Milwaukee County Nursing Home Association. Two similar programs were given in the years following, and in 1954 a statewide workshop was held in Milwaukee in cooperation with the Marquette College of Nursing and the State Nursing Home Association. Another statewide program was held in 1955, conducted jointly by the central agency, the University of Wisconsin Extension Department, the State Health Department, and the State Nursing Home Association; similar workshops have been given up to the present.

The central agency has compiled and published a small fact booklet on the patients in Milwaukee's proprietary nursing homes. The booklet gives statistical information on age, sex, diagnoses, types of care required, referral sources, patient income, and costs of care. These data were obtained with a special questionnaire used by the staff worker in the course of her routine nursing home visits.

Other informational and educational material published and distributed by the agency includes a brochure on the important problems of chronic illness written for the general public, a 12-page booklet giving some of the general points to be considered by patients and their families in selecting a nursing home, and a similar booklet highlighting some of the essential problems in the operation of a nursing home, directed toward administrators of these facilities.

A recent project has been the mailing of a quarterly "Food Notes" bulletin to nursing home operators and cooks. This 2-to-4-page bulletin, which is prepared with the help of the Milwaukee Health Department nutritionist, notes some of the plentiful and easily obtained foods in a particular season, gives suggestions for their use in menus, and contains recipes in serving quantities for from 10 to 50 persons. Suggestions are also given on attractive and efficient serving methods, special dishes, and the like.

TABLE 2.—*Nature of Requests from Oct. 1, 1957, to Sept. 30, 1958*

	New Cases	Recalls*	Total
Nursing Home, boarding home, institution	517	154	671
Housekeeper, attendant, etc.	34		34
Information re facilities and resources			
Sheltered or home employment	47		47
Financial assistance	15		15
Wheel chairs, hospital beds, etc.	9		9
Rehabilitation services	5		5
Free or cheaper medicine	2		2
Housing	6		6
Transportation to clinics	2		2
Day care (custodial)	45		45
Restaurant serving special diets	3		3
Establishing new facility	79		79
Consultation, educational material	246		246
Counseling	277		277
Additional information only	141		141
Total	1,428	154	1,582

* Persons previously receiving service from agency

The director of the central agency is co-author of a book on the care and rehabilitation of the chronically ill; she continues to write articles and develop exhibits, literature for distribution, and other educational material on the general and specific problems of the chronically ill and their care.

The central agency is currently investigating the possibilities for future study and action in such areas as encouraging the development of new skilled nursing care facilities by church and other nonprofit groups, who have not been too active in this field in the past, possible contributions by the general hospital in improving long-term care, improved methods of caring for the homebound chronically ill, and a study of the incidence of chronic disease in certain special groups, such as the Negro population and industry. The agency continues to work toward fostering an enlightened public attitude toward the problems of the aged and chronically ill and to stimulate the coordination of community facilities and services in meeting these problems.

MEDICAL NEWS

ARIZONA

Annual Meeting in Chandler.—Preliminary plans for the 68th annual meeting of the Arizona Medical Association in Chandler, April 30-May 2, were announced by Dr. Dermont W. Melick, of Phoenix, chairman of the scientific assembly committee. Papers will be presented by Drs. Haddon M. Carryer, Mayo Clinic; John W. Cline, Stanford University; Harold D. Jenkins and Marvin E. Johnson, University of Colorado; Henry H. Kessler, Kessler Institute for Rehabilitation; Johannes M. Nielsen, University of California at Los Angeles School of Medicine; and Thomas L. Royce, Baylor University. As a special feature, a medical education workshop will be held May 1. Presentations on medical education will be given by Dr. John Z. Bowers, University of Wisconsin; Fred Dow Fagg Jr., Ph.D., president, Western Interstate Commission for Higher Education; Mr. Reuben Gustavson, president, Resources for the Future; Walter L. Hard, Ph.D., University of South Dakota; and Drs. Marvin E. Johnson, University of Colorado; Vernon W. Lippard, Yale University; Roscoe L. Pullen, University of Missouri; Thomas L. Royce, Baylor University; and Thomas B. Turner, Johns Hopkins University. Moderator will be Dr. John W. Cline, Stanford University. The meeting will be held in the San Marcos Hotel. Officers of the association are Dr. Wilkins R. Manning, Tucson, president; Dr. Dermont W. Melick, Phoenix, president-elect; Dr. Lindsay E. Beaton, Tucson, vice-president; Dr. Leslie B. Smith, Phoenix, secretary; and Dr. Clarence E. Yount Jr., Prescott, treasurer.

ARKANSAS

Annual Session Planned at Fort Smith.—The 83rd annual session of the Arkansas Medical Society will be held April 12-15 at the Goldman Hotel, Fort Smith. The president's address will be given the morning of April 13 by Dr. Louis K. Hundley, Pine Bluff. "Third Party Payment for Medical Care" will be presented by Dr. Frank C. Coleman, Des Moines, president, College of American Pathologists, that afternoon. Out-of-state speakers include the following:

Drs. Harold O. Perry, Rochester, Minn.; Lt. Col. George R. Steinkamp, M.C., U. S. A. F.., Randolph AFB, Texas; I. Frank Tullis, Memphis, Tenn.; J. E. Markee, Durham, N. C.; M. T. Jenkins, Dallas, Texas; Conrad G. Collins and Edgar Burns, New Orleans; Hugh F. Hare and Howard House, Los Angeles; Harris D. Riley, Oklahoma City, Okla.; William Dameshek and Kenneth W. Warren, Boston.

Specialty section meetings are planned for April 14, with the annual banquet to be held that evening. Dr. F. J. L. Blasingame, Executive Vice-President, American Medical Association, will address the House of Delegates the afternoon of April 12. Films and exhibits are arranged. Entertainment includes a golf tournament. For information write Mr. Paul C. Schaefer, Kelley Bldg., Fort Smith, Ark., Executive Secretary.

COLORADO

Plan Expansion of Tuberculosis Research Facilities.—The Colorado Foundation for Research in Tuberculosis, housed in the Webb building on the University of Colorado Medical Center campus, Denver, will add a third floor to the structure to expand its facilities for research in biochemistry and the genetics of bacteria. Dr. Roger S. Mitchell, director of the foundation, said the organization has the necessary funds to move forward with construction as soon as the Board of Regents approves the details. He added that Dr. Oscar Reiss, of the Johns Hopkins University School of Medicine, Baltimore, will join the staff in June to head this new activity. The Colorado Foundation for Research was established in Colorado Springs in 1922 by the late Dr. Gerald E. Webb, and was moved to the Medical Center campus in 1954. Dr. James J. Waring, professor of medicine emeritus, at the School of Medicine, is the foundation president.

DISTRICT OF COLUMBIA

Dedicate Hospital Research Center.—On March 22 Children's Hospital of the District of Columbia dedicated its new Children's Hospital Variety Club Research Center. Dedication speaker was Dr. Leroy E. Burney, Surgeon General, U. S. Public Health Service. The research center, located next to the hospital, at 12th and W Streets, N., was built at a cost of about $800,000, financed in part by grants totaling $484,000 and by a contribution of $200,000 from the Variety Club of Washington. Additional funds are being raised in a campaign for $460,000 launched last November. The Children's Hospital Variety Club Research Center, which commemorates the Variety Club's Chief Barker, Fred S. Kogod, is a modern building with three floors and a basement. The front is of heavy, opaque glass

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

and aluminum, and the sides are of brick to complement existing hospital buildings. In the air-conditioned building all necessary services (water, electricity, gas, compressed air) will be available in each research unit. Movable partitions will allow rearrangement of research areas without extensive repairs and remodeling. In addition to the laboratories of the seven research sections there is a radioisotope laboratory and a large sterilizing room with equipment for washing and sterilizing glassware. The Research Foundation of Children's Hospital was incorporated in 1947 to further pediatric research at Children's Hospital. Its president is Dr. Edgar W. Davis, and the director of the foundation is Dr. Robert H. Parrott, physician-in-chief of Children's Hospital.

HAWAII

Annual Convention in Hilo.—The Hawaii Medical Association will hold its 103rd annual meeting in Hilo April 23-26 at the American Legion Hall. Panel discussions on "Coping with the Teenager" and "Hernia Hydrocele and Undescended Testicle" will be moderated by Drs. J. Roswell Gallagher, Boston, and Tague C. Chisholm, Minneapolis, respectively. The following papers are scheduled:

Rehabilitation of the Hemiplegic, Dr. R. Frederick Shepard.
Cerebral Hematoma, Dr. John J. Lowrey.
Portal Hypertension, Experiences in the Management of Hemorrhage from Esophageal Varices, Dr. Gilbert C. Freeman.
Improving Medical Certifications of Death, Dr. Halbert L. Dunn.
Pitfalls in Surgery of the Hand, Dr. Leabert R. Fernandez.
Surgical Approach to Fascial Space Infection in the Hand, Dr. Raymond G. Chang.
Study of Lipoproteins in the Nisei, Dr. Kyuro Okazaki.
Report on Coronary Atherosclerosis in our Different Ethnic Groups from a Successive Series of 2,000 Autopsies, Dr. Nils P. Larsen and Dr. Walter M. Bortz.

The presidential address will be given by Dr. William N. Bergin. Exhibits are planned, and the annual golf tournament will be held April 26. Woman's auxiliary activities include a golf tournament April 25. Registration fee is $10.

ILLINOIS

Chicago

Visiting Pathologist.—Dr. R. Winston Evans, pathologist of Liverpool, England, has started teaching as temporary visiting professor of pathology at the University of Chicago. He is lecturer in the department of clinical pathology at the University of Liverpool and a consultant pathologist at the David Lewis Northern Hospital and the St. Paul's Hospital in Liverpool.

Dr. Jensen Receives Pasteur Award.—Lloyd B. Jensen, Ph.D., was chosen to receive this year's Pasteur Award, the Society of Illinois Bacteriologists announced. Formal presentation of the sterling silver medal and cash award will be made April 11 at a dinner meeting of the society in the Morrison Hotel. The Pasteur Award is given for "notable contributions to the science of bacteriology." The award is given to Dr. Jensen "for his outstanding contributions to food microbiology." For 27 years prior to retirement in April, 1958, he was chief bacteriologist at Swift and Company. He also lectured for 16 years at the U. S. Army Meat and Dairy Hygiene School on Pershing Road. In 1954 he was appointed consultant to the Walter Reed Army Institute of Research by the Surgeon General. Dr. Jensen was one of the founders and early editors of the journal, *Food Research.*

Appoint Dr. Kronfeld Department Head.—Appointment of Dr. Peter C. Kronfeld, of Wilmette, as professor and head of the department of ophthalmology, University of Illinois College of Medicine, was approved March 12 by the board of trustees. Dr. Kronfeld also was named ophthalmologist-in-chief of the University of Illinois Hospital and the Illinois Eye and Ear Infirmary. He has been professor of ophthalmology at the U. of I. College of Medicine and attending ophthalmologist at the infirmary since 1947. He joined the faculty of the university's professional colleges in 1943. Dr. Kronfeld succeeds Dr. William F. Hughes, also of Wilmette, who resigned the positions last September, but has continued on the College of Medicine staff as clinical professor of ophthalmology. Dr. Howard L. Wilder, assistant professor of ophthalmology, has been acting head of the department. Dr. Kronfeld received his M.D. from the University of Vienna and joined the staff of the University of Chicago in 1927 and remained there until 1933.

KANSAS

Annual Lecture Given.—The annual Clendening Lecture at the University of Kansas School of Medicine, Kansas City, was delivered by Dr. Edward H. Hashinger, professor emeritus of medicine and gerontology, on March 12. "Arthur E. Hertzler—the Kansas Horse and Buggy Doctor" was the subject of his tribute to the Kansas physician who was on the faculty of the school for over 30 years prior to his death in 1946. The Clendening series was established in 1949 by the widow of the late Dr. Logan Clendening, a pioneer in medical education at the Kansas School. Dr. Hashinger had residency training in the Halstead, Kansas, Hospital founded by Dr. Hertzler, who received international recognition for his best-seller, "The Horse and Buggy Doctor."

MASSACHUSETTS

Dr. Fulton Named First Warren Professor.—Prof. George P. Fulton, Ph.D., of Lexington, chairman, department of biology, Boston University's College of Liberal Arts, was named to the first Shields Warren Professorship at Boston University, according to an announcement by President Harold C. Case. The chair was established a year ago on the occasion of the 60th birthday of Dr. Shields Warren, of West Newton, pathologist and chairman of the executive committee of the Boston University board of trustees. At that time, some 700 Greater Bostonians donated funds to establish the professorship at Boston University, in honor of Dr. Warren, whose grandfather was the university's first president. Dr. Fulton was a pioneer in the use of the hamster cheek pouch method of studying the small blood vessels. Last year, Dr. Fulton was a visiting professor of physiology at the Stanford University School of Medicine in San Francisco for seven months. He is associate editor of *Angiology* and a fellow and vice-president of the American College of Angiology.

MICHIGAN

Annual Cancer Day in Flint.—The Genesee County Medical Society will present its 14th annual Cancer Day, April 22, at the Merliss Brown Auditorium, Hurley Hospital, Flint. Dr. Jackson E. Livesay, president of the society, will open the meeting with an address. Presiding officers at the forenoon and afternoon sessions will be Drs. G. B. Saltonstall, president, Michigan State Medical Society, Charlevoix, and James W. Logie, president, Kent County Medical Society, Grand Rapids. Topics and speakers are as follows:

The Current Status of Interstitial Irradiation, Dr. Ulrich Henschke, New York City.
Head and Neck Cancer as Seen in the Oral Cavity, Dr. Danely P. Slaughter, Chicago.
The Current Status of Cancer Research, Dr. Freddy Homburger, Cambridge, Mass.
The Problem of Soft Tissue Tumors as Seen by the Surgical Pathologist, Dr. Raffaele Lattes, New York City.
Extended Operations for Cancer of the Stomach and Colon and the Second Look, Dr. Owen H. Wangensteen, Minneapolis, Minn.
The Problem of Pigmented Mole and Malignant Melanoma, Dr. George T. Pack, New York City.

MISSISSIPPI

Annual Meeting of State Psychiatrists.—The newly formed Mississippi Psychiatric Society, a district branch of the American Psychiatric Association, held its first annual meeting on March 7 at the University of Mississippi Medical Center, Jackson. Dr. J. G. N. Cushing of Baltimore, southern area representative on the policy committee of the Assembly of District Branches, addressed the group on historical aspects of the American Psychiatric Association and the formation of district branches. Dr. Hamilton F. Ford, of the University of Texas Medical Branch, Galveston, gave the academic lecture on "Phrenotropic Drugs—Applicability Based on Chemical Grouping." Dr. Floy Jack Moore, chairman, department of psychiatry, University of Mississippi Medical Center, was elected president to succeed Dr. Frank A. Donaldson, of Jackson. Others elected as the first complete slate of officers were: president-elect, Dr. Lawrence G. Behan, Gulfport; secretary-treasurer, Dr. L. C. Hanes, Jackson; council member, Dr. John J. Head, Whitfield; delegate to assembly of district branches, Dr. William L. Jaquith, Whitfield; and alternate delegate, Dr. Beverley E. Smith, Jackson.

MISSOURI

Hospital Lecture.—The Jewish Hospital of Saint Louis announced that the 12th Jack H. Tritt Memorial Lecture was given April 2 by Dr. Edwin P. Hiatt, chief, Aero Medical Laboratory, Wright Air Development Center, Dayton, Ohio, on "Medical Problems of Manned Space Flight."

NEBRASKA

Student Aid Fund Established.—A fund to aid needy students in medicine has been established by a group of physicians at the University of Nebraska College of Medicine, Omaha. The charter members are all on the staff of the university. A nonprofit corporation without capital stock, the Nebraska Medical Education Fund, Inc., is "for educational and charitable purposes." Aid will be given regardless of race or creed. The main purpose of the organization is "to help needy and worthy students in medical and health professions to obtain higher education." The corporation has the authority to accept contributions and invest them, borrow money, and pay and obligate itself for any expenses involved. Loans to one student for one academic year may not exceed $1,500. Applications can be obtained from the Student Assistance Committee through the office of the assistant dean. To be a member with full voting rights, one must be licensed to practice medicine in Nebraska. However, honorary members may be named. Officers of the corporation are Dr. Clinton C. Millett, president; Dr. Willson B. Moody, vice-president; and Dr. John R. Schenken, treasurer.

NEW YORK

State Society Convenes in Buffalo.—The Medical Society of the State of New York will hold its 153rd annual convention May 9-15 at the Hotel Statler–Hilton, Buffalo. The annual dinner, at which Dr. Gunnar Gundersen, President, American Medical Association, will be the principal speaker, will take place the evening of May 11. The program will consist of general sessions, sections, exhibits, and films. Symposiums and panel discussions on Surgery in Cardiovascular Disease, Prognosis in Surgically Treated Cancer, Hypnosis in Clinical Practice, and the Role of the General Hospital in the Care of Special Medical Problems are planned.

A session on the History of Medicine is set for May 15, 9 a. m., at which time the section on legal medicine will open. The opening session of the regular annual meeting of the House of Delegates will be convened at 10 a. m., May 9, by the speaker, Dr. Joseph A. Lane, of Rochester. At this session Dr. John D. George Sr., of Verona (Oneida County), will receive the State Medical Society award as "Outstanding General Practitioner of New York State for 1958." At the annual dinner, the president's medal will be awarded to Dr. Leo E. Gibson, of Syracuse. He will be succeeded by Dr. Henry I. Fineberg, of Jamaica (Queens County, New York City).

Report on Health Statistics.—A record 362,000 births were reported in New York during 1958; the death rate, 10.4 per 1,000 population, was the third lowest in the history of the state; the tuberculosis death rate, 8.1 per 100,000 was an all-time low; and mortality from cancer was the lowest in eight years. This information is contained in "New York's Health," the 1958 annual report of the New York State Health Department available for distribution. Dr. Herman E. Hilleboe, state health commissioner, explained that the climb in birth rates and the declining death rates have combined since 1950 to increase the population of the state by 1,500,000 persons, giving impetus to the establishment of full-time county health departments. During the year Monroe, Dutchess, and Chemung counties began operation of such units; seven counties with 100,000-plus populations have yet to do so. Advances cited in the report include the work being done at Roswell Park Memorial Institute and the State Rehabilitation Hospital at West Haverstraw; establishment of a 15-station air sampling network by the Air Pollution Control Board; conducting baseline surveys of natural radiation; further development of the state-wide meat inspection program; activities in the field of environmental sanitation, medical services, and local health service; and the research and service activities of the department's Division of Laboratories and Research.

New York City

Dr. DeVoe Named Department Chairman.—The appointment of Dr. Arthur G. DeVoe as professor and chairman of the department of ophthalmology, Columbia University College of Physicians and Surgeons, was announced March 15. At the same time, the appointment of Dr. DeVoe as attending ophthalmologist and director of the ophthalmology service in Presbyterian Hospital was announced. The appointments are effective July 1, when Dr. John H. Dunnington retires from those posts. Dr. DeVoe was a resident in ophthalmology at the Institute of Ophthalmology at Presbyterian Hospital from 1937 to 1940. He served as an associate in ophthalmology in the College of Physicians and Surgeons from 1940 until 1950, when he became professor and chairman of the department of ophthalmology in the New York University Post-Graduate Medical School.

Personal.—Dr. Nadene Coyne has been appointed coordinator of training for physicians in the department of physical medicine and rehabilitation of New York University-Bellevue Medical Center and director of the Respirator Center at Goldwater Memorial Hospital. She was formerly director of the department of physical medicine and rehabilitation, Cleveland General Hospital, Cleveland.—Dr. James A. Brussel, assistant commissioner, New York State Department of Mental Hygiene, will have his novel, "Just Murder, Darling," published by Charles Scribner's Sons; July release is anticipated. Dr. Brussel is also completing "Psychiatry for the Layman" for Barnes and Noble.—Dr. Alexander B. Gutman, director, department of medicine, Columbia University College of Physicians and Surgeons, delivered the annual John Auer lecture sponsored by Phi Beta Pi medical fraternity, Saint Louis University School of Medicine, March 13.

Visit by Foreign Public Health Physicians.—An international group of 26 graduate physicians pursuing advanced studies in public health at Harvard visited the State University of New York Downstate Medical Center, Brooklyn, March 18 and 20 to observe the teaching and research program in environmental medicine. The group was led by Dr. Brian MacMahon, head, department of epidemiology at Harvard. Representing 13 countries in North and South America, Europe, and Asia, the group included 18 physicians who will be returning to faculty positions in preventive medicine in their own countries as well as eight physicians taking the advanced degree program in epidemiology. For some of the group, the visit to the Downstate Medical Center is part of a "peripatetic seminar" program which will include visits to other preventive medicine teaching centers in the United States, the United Kingdom, Puerto Rico, Yugoslavia, and Lebanon.

Dr. Goldwater Honored.—Dr. Leonard J. Goldwater, professor of occupational medicine, Columbia University School of Public Health and Administrative Medicine, received an award from the President's Committee on Employment of the Physically Handicapped and the New York State Governor's Committee on "Employ the Physically Handicapped" March 19 "for contributions in eliminating prejudice and misinformation regarding the rehabilitation of heart patients." The nomination submitted for Dr. Goldwater cited him for his work in organizing the Cardiac Work Classification Unit at Bellevue Hospital in New York City in

1941. This unit was designed to study employment problems of cardiac patients and to study the effects of employment on heart disease and the effects of heart disease on the ability to work. Dr. Goldwater was installed recently as president of the American Academy of Occupational Medicine. He is a member of the World Health Organization expert advisory panel on social and occupational health and is a consultant to the office of vocational rehabilitation, Department of Health, Education, and Welfare.

Scholarship for Advanced Study Abroad.—In the current year the Committee on Medical Education, New York Academy of Medicine, will award one scholarship grant in the amount of $4,500 for the academic year 1960-1961. This scholarship was established to provide aid for advanced study abroad in a clinical subject in preparation for the practice of medicine or surgery in any of their branches. As stipulated by the donor, candidates must be male interns or residents in voluntary, municipal, or Veterans Administration hospitals in New York City. The course of study, the auspices under which it is to be taken, and the place or places where the study is to be pursued must receive the approval of the committee. Applicants are favored who, from their records, show themselves capable of advanced work in clinical medicine. The committee stipulates that the study be pursued abroad, preferably in Great Britain or in continental Europe. Applications for this scholarship must be submitted by Sept. 1. Candidates may secure application forms by writing: Dr. Robert L. Craig, Executive Secretary, Committee on Medical Education, The New York Academy of Medicine, 2 E. 103 St., New York 29.

NORTH CAROLINA

Appropriations for Public Health.—The Raleigh *News and Observer* has reported that per capita state appropriations for public health in some of the Southern states for 1958 were as follows: Georgia, $1.73; Florida, $1.49; Virginia, $1.27; Kentucky, $0.98; Tennessee, $0.89; South Carolina, $0.85; Mississippi, $0.81; and North Carolina, $0.70. While local health departments in North Carolina were established on a basis whereby the state and county share the expenses equally, it is said that the state has gradually lagged in its support of this work until now the counties bear 77% of the cost, the state only 17%, and the remaining 6% comes from other sources.

Scholarships for Medical Study.—Winners of the second eight Reynolds Scholarships for study at Bowman Gray School of Medicine have been announced by Dr. C. C. Carpenter, executive dean. The scholarships, provided by the A. Smith Reynolds Foundation, are adequate to cover the cost of a medical education, including four years of medical school and two years of postgraduate hospital training. Benefits range from $2,400 to $4,800 a year. Reynolds Scholars are chosen by the Committee on Admissions from residents of North Carolina who are admitted to the next entering class at Bowman Gray. Selection is based on character, scholarship, potential as a physician, and financial need. The recipients must have the intention to practice medicine in North Carolina for at least five years after completing their medical education. The first eight Reynolds Scholars will complete the freshman year at Bowman Gray in June. The second eight will enroll in September.

Conference for Medical Record Personnel.—A Conference on Medical Records will be held April 27-29 at the Duke University Medical Center. Planned for hospital medical record personnel and hospital administrators, the conference will be sponsored by Duke in cooperation with the Association of Medical Record Librarians of North Carolina. The second day of the conference will be designed especially for hospital administrators as well as for medical record personnel. Guest speakers who will join Duke Medical Center staff members in presenting the conference program include Margaret J. Heath, president, American Association of Medical Record Librarians, Buffalo, N. Y.; Howard M. Kline, chief, Education and Training Branch, Division of International Health, U. S. Public Health Service, Washington, D. C.; Margaret C. Doran, chief, Medical Record Library Division, Veterans Administration Department of Medicine and Surgery, Washington, D. C.; Donald Smith, administrative assistant, Medical Education for National Defense, Washington, D. C.; Dr. Robert R. Cadmus, director N. C. Memorial Hospital, Chapel Hill; Sample B. Forbus, administrator, Watts Hospital, Durham; and Margaret L. Russell, president, N. C. Association of Medical Record Librarians, Winston-Salem. The conference will be open to North Carolina and to out-of-state medical record personnel and hospital administrators. For information, write Mrs. Je Harned Bufkin, Medical Record Library, Duke University Medical Center, Durham, N. C.

PENNSYLVANIA

Tuberculosis Meeting in Scranton.—The Pennsylvania Tuberculosis and Health Society will hold its annual meeting in collaboration with the Pennsylvania Trudeau Society, Pennsylvania Chapter, American College of Chest Physicians, and the Pennsylvania Conference of Tuberculosis Workers April 15-17 in Scranton. The meeting is acceptable for five hours of category II credit by the American Academy of General Practice. Dr. David A. Cooper will preside at a "Consecutive Case Conference" the morning of April 16. A discussion, "A New Challenge: Respiratory Diseases," is planned for April 15. Coffee conferences the morning of April 17 will have the following titles and participants:

Tuberculosis, Drs. John S. Packard, Milton, John C. Sanner, Scranton, and Samuel C. Stein, Philadelphia.
Emphysema, Drs. Richard T. Cathcart and Henry P. Close, Philadelphia.
Silicosis, Drs. Ross K. Childerhose, Harrisburg, and Peter A. Theodos, Philadelphia.
Other Acute Respiratory Diseases, Drs. Harold L. Israel and Robert L. Mayock, Philadelphia.

A panel on "Social Implications of a Changing Tuberculous Population" will be conducted the morning of April 16.

Philadelphia

Plan Alumni Publication.—*Medical Affairs,* a new medical alumni and faculty publication has been launched jointly by the School of Medicine and Graduate School of Medicine of the University of Pennsylvania. It will be published four times a year in the spring, summer, fall, and winter. *Medical Affairs* will not be a scientific publication. It will contain editorials by leaders in fields of interest related to medicine, articles by faculty and alumni, news of developments at the schools, news of alumni, book reviews, and activities of the faculty members. More than 14,000 copies will go to Pennsylvania medical alumni in 50 states and around the world. The editorial office of *Medical Affairs* is located at 201 S. 34th St., Philadelphia 4.

Symposium on Structure of Science.—A symposium on "The Structure of Science" will be held April 17-18 accompanying the formal opening of new laboratories and a new museum at the Wistar Institute of Anatomy and Biology. Senator Lister Hill, of Alabama, and Dr. LeRoy Burney, surgeon general, U. S. Public Health Service, will be among the speakers. Mayor Richardson Dilworth will discuss Philadelphia as a center for basic research. The symposium will be held in Irvine Auditorium, University of Pennsylvania, and the institute will be the scene of a reception and a tour of its new laboratories and museum April 18, following the afternoon session. Papers by foreign participants include: "Theories of Tolerance," Dr. Peter B. Medawar, Jodrell professor of zoology, University College, London; "The Structure of Viruses," Dr. Francis H. C. Crick, member of the medical research council's unit for molecular biology at Cavendish Laboratories, Cambridge, England; "Chemical Structure and Biological Function," Dr. H. Gobind Khorana, head of organic chemistry, British Columbia Research Council, University of British Columbia; "The Evolution of Tumor Cell Populations," Dr. George Klein, professor of tumor biology at Karolinska Institute, Stockholm, Sweden. The Wistar Institute was founded in 1818 as the Wistar Museum. The museum was expanded into a biological research institute in 1892 in consequence of gifts from Gen. Isaac J. Wistar, grand-nephew of the founder. The Wistar Institute of Anatomy and Biology was formally opened in 1894. The original institute building has been completely reconstructed during the past two years to provide new laboratories and a new museum.

TENNESSEE

Grant for Brain Research.—One million dollars for a five-year study on prevention of brain damage has been awarded to the University of Tennessee College of Medicine by the National Institute of Neurological Disease and Blindness, U. S. Public Health Service. Announcement of the largest grant the medical units have ever received was made by Dr. O. W. Hyman, vice-president in charge of the medical units, and Dr. Maston K. Callison, dean of the college. Funds will be available at the rate of more than $200,000 per year. Dr. James G. Hughes, professor of pediatrics, will be principal investigator, and Dr. Phillip C. Schreier, professor of obstetrics and gynecology, co-investigator. The Memphis study will involve close cooperation between several departments in the college. More than 40 people will be on the research team. About 750 women and their babies in units of City of Memphis Hospitals will be studied for five years. The local project is part of a collaborative effort in which 15 medical schools in the nation will participate, simultaneously collecting information on causes of brain damage. Information from the schools will be pooled, and it is expected that by the end of five years the schools will have studied more than 60,000 pregnant women and their offspring.

Annual Meeting in Memphis.—The 124th annual meeting of the Tennessee State Medical Association will be held April 12-15 in Memphis, with headquarters at the Peabody Hotel. Guest speaker at the president's banquet, April 13, 7 p. m., with Dr. James C. Gardner, president, presiding, will be Robert J. Farley, LL.B., dean of the School of Law, University of Mississippi, Oxford. At the General Practice Day session that day, a symposium, "Peripheral Vascular Disease—Its Management," will be moderated by Dr. Harwell Wilson. Special society meetings will be held each day. Papers by out-of-state speakers to be presented at the general sessions are as follows:

The Role of the Anesthesiologist in the Practice of Medicine, Dr. Scott M. Smith, Salt Lake City, Utah.
Antibiotic Resistant Staphylococcic Disease, Dr. William Sandusky, Charlottesville, Va.
The Pathology of Low Back Pain, Dr. Walter C. J. Putschar, Washington, D. C.
Infertility—A Family Unit Problem, Dr. William H. Masters, St. Louis.
The Newer Oral Antidiabetic Agents, Dr. Rachmiel Levine, Chicago.

A second symposium, "Diuretics," is scheduled for the morning of April 14. Scientific and technical exhibits are planned. For information, write the Tennessee State Medical Association, 112 Louise Ave., Nashville 5, Tenn.

TEXAS

Annual State Meeting in San Antonio.—The 92nd annual session of the Texas Medical Association will be held April 18-21 in San Antonio, with headquarters at the Hilton Hotel. Among the papers to be presented are "Abnormal Uterine Bleeding at or After the Menopause," Dr. Newell W. Philpott, Montreal, Canada, professor of obstetrics and gynecology, McGill University Faculty of Medicine, and "Land of the Free and Easy," by Dr. Gunnar Gundersen, La Crosse, Wis., President, American Medical Association. Other guest speakers include the following:

Drs. Walter C. Alvarez and Edward I. Compere, Chicago; George C. Andrews, John M. McLean, and Byron Smith, New York City; Harry E. Bacon and James E. Eckenhoff, Philadelphia; Richard J. Bing, St. Louis; Murray M. Copeland and Oscar B. Hunter Jr., Washington, D. C.; John B. Erich, Rochester, Minn.; Jack R. Ewalt, Donald D. Matson, Duncan E. Reid, and Kenneth W. Warren, Boston; Grace A. Goldsmith, New Orleans; Eugene A. Hargrove, Raleigh, N. C.; Herman E. Hilleboe, Albany, N. Y.; Ted F. Leigh, Atlanta, Ga.; Champ Lyons, Birmingham, Ala.; Mitchell I. Rubin, Buffalo, N. Y.; O. A. Sander, Milwaukee, Wis.; and John T. Sessions Jr., Chapel Hill, N. C.

Section meetings, motion picture sessions, and scientific and technical exhibits are arranged. The annual golf tournament will be held April 20. President of the Texas Medical Association is Dr. Howard O. Smith, Marlin. For information write Mr. C. L. Williston, 1801 N. Lamar Blvd., Austin, Texas, Executive Secretary.

GENERAL

Award for Work on Obstetrics or Gynecology.—The Central Association of Obstetricians and Gynecologists is offering an award of $250 for outstanding investigative or clinical work in obstetrics or gynecology. Any accredited physician, research worker, or medical student living within the geographic confines of the Association is eligible. Papers must be written expressly for this competition and must be original. The winning paper will be presented at the annual meeting Sept. 24-26 in Chicago. Manuscripts should be submitted to the secretary in triplicate, accompanied by an abstract not to exceed 150 words. No author's identification shall be shown on any of the three copies, the only identification being a covering letter addressed to the secretary. Papers should be in the hands of the secretary by June 25 and should be addressed to: Dr. Edwin J. DeCosta, Secretary, Central Association of Obstetricians and Gynecologists, 104 S. Michigan Ave., Suite 615, Chicago 3.

Urological Meeting in Atlantic City.—The 54th annual meeting of the American Urological Association, Inc., will be held April 20-23 at the Chalfonte-Haddon Hall, Atlantic City, N. J., under the presidency of Dr. Adolph A. Kutzmann, Los Angeles, who will present the presidential address the afternoon of April 22. Over 25 papers are scheduled for presentation with discussions following. Dr. Hans J. Klapproth, Cleveland, will present "Distribution of Renal Arterial Circulation in the Dog" the morning of April 21 as the first prize essay contest lecture. A program of motion pictures and scientific and technical exhibits are arranged. The Ramon Guiteras Lecture, "Explants of Genito-Urinary Tissues Cultivated for Experimental Studies," will be given by C. M. Pomerat, director, Tissue Culture Laboratory, University of Texas Medical Branch, Galveston. Panel discussions on "Carcinoma of the Bladder" and "The Prostatic Nodule" are arranged. Dr. Einar Ljunggren, Goteborg, Sweden, will present "Some Aspects of Renal Tumors" the afternoon of April 23.

Experimental Biology Meeting in Atlantic City.—The 43rd annual meeting of the Federation of American Societies for Experimental Biology will be held in Atlantic City, N. J., April 13-17. The federation is comprised of the American Physiological Society, the American Society of Biological Chemists, the American Society for Experimental Pathology, the American Society for Pharmacology and Experimental Therapeutics, the American Institute of Nutrition, and the American Association of Immunologists. Headquarters hotel for the federation will be the Traymore. An opening joint session will be held April 14, 8 p. m., under the title "The Biological Significance of the Fine Structure of Macromolecules," with Dr. Francis H. C. Crick, Cambridge, England, as chairman, and including a paper by Dr. J. C. Kendrew, Cavendish Laboratory, Cambridge, England, on "Structure and Function in Myoglobin and Other Proteins." Intersociety sessions under the titles "Physiology and Drug Actions," "Nutritional Requirements of Animal Cells Cultivated in Vitro," and "Neurochemistry" (two sessions) will include the following section titles: Neurochemistry, Atherosclerosis, Blood Clotting, Tissue Culture, Cytology, Neuropharmacology, and Radiation. A program of motion pictures will be presented April 13. Industrial scientific exhibits are planned.

World Conference on Medical Education.—Plans for the second World Conference on Medical Education, to be held in Chicago Aug. 29-Sept. 4, were discussed recently. The seven-day conference, sponsored jointly by world medical bodies, including the World Medical Association, is arranged "to provide a common ground for the free exchange of scientific information and experiences between countries." Collaborating with the W. M. A. in sponsoring the conference are the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities. President Eisenhower, who helped organize the National Fund for Medical Education, is patron of the conference. Serving as conference president will be Dr. Raymond B. Allen, chancellor, University of California, Los Angeles. To be held in the Palmer House, the conference will have 125 speakers from about 50 countries, and all business, including lectures, will be translated simultaneously into English, French, and Spanish. "Medicine—A Lifelong Study" is the conference theme. For information write Mrs. Clara Lewinter, World Medical Association, 10 Columbus Circle, New York 19.

Meeting in Chicago to discuss plans for the second World Conference on Medical Education were (left to right): Dr. W. C. Bornemeier, Chicago; Dr. Glen R. Shepherd, assistant secretary, Council on Medical Education and Hospitals, A. M. A.; Miss Margaret Natwick, executive assistant, W. M. A.; Thomas R. Gardiner, co-chairman of the technical exhibits; Dr. Robert A. Moore, dean, College of Medicine in Brooklyn, State University of New York; Dr. George F. Lull, retired secretary and general manager, A. M. A.; Dr. Myron E. Wegman, secretary general, Pan American Sanitary Bureau; Mrs. Clara Lewinter, executive secretary of the conference; Dr. Victor Johnson, director, Mayo Foundation for Medical Education and Research; and Dr. Louis H. Bauer, Secretary General of the World Medical Association.

Government Awards for Lecturing and Research.—U. S. Government Awards for 1960-61, authorized by Public Law 584, 79th Congress, The Fulbright Act, under the auspices of the Board of Foreign Scholarships and the Department of State, were announced. These awards are available for university lecturing and for advanced research in Latin America (Argentina, Brazil, Chile, Colombia, Ecuador, Peru); South and Southeast Asia (Burma, India, Pakistan, Philippines, Thailand); and Pacific Area (Australia, New Zealand). Eligibility includes U. S. citizenship; at least one year of college or university teaching experience (for lecturing); a doctoral degree for research or recognized professional standing (candidates for the degree should apply to the Institute of International Education, 1 E. 67th St., New York City); in some cases, a knowledge of the language of the host country. Awards will be tenable in one country, usually for an academic year, and payable in currency of host country. Round-trip travel for the grantee will be provided but not for members of his family. A maintenance allowance to cover ordinary living expenses of the grantee and his family while in residence abroad and a small incidental allowance for travel, books, and services required in performance of assignment will be given. Closing date of application is April 25. For application forms and information write: Conference Board of Associated Research Councils, Committee on International Exchange of Persons, 2101 Constitution Ave., Washington 25, D. C.

Psychiatrists Meet in Philadelphia.—The American Psychiatric Association will hold its 115th annual meeting at Convention Hall Auditorium in Philadelphia April 27-May 1. Dr. Francis J. Gerty, Chicago, president of the association, will call the meeting to order the morning of April 27. Over 160 papers will be presented, including the following by foreign authors:

A Cross-Cultural Approach to Mental Illness, Dr. Eric D. Wittkower and J. Fried, Ph.D., Montreal, Canada.
Further Developments in the Day Hospital, Dr. T. J. Boag, Montreal.
The Practice of Psychiatry in England Under the National Health Service, Dr. A. Spencer Paterson, London.
A Family Programme for First Year Medical Students, Dr. J. S. Tyhurst, Vancouver, British Columbia.
Socio-Economic Factors in Discharge of Long-Term Mental Hospital Patients, Dr. Gordon O. Patton, Quebec, Canada.
Types of Marital Complementarity and Emotional Health of Children, Dr. Nathan B. Epstein and William A. Westley, Ph.D., Quebec.
A Follow-Up Study of Two Groups of Veterans: (a) Five Years (b) Ten Years, Treated with Sub-Coma Insulin at a Montreal Veterans Hospital, Dr. Harry Grauer, Montreal.

Two dozen evening round-table meetings are planned. Dr. Karl A. Menninger, Topeka, Kan., will give the Academic Lecture. The Adolf Meyer Research Lecture will be given by Dr. W. Grey Walter, Bristol, England. For information, write the American Psychiatric Association, 1700 18th St., N. W., Washington 9, D. C.

Meeting of Physicians in Chicago.—The American College of Physicians will meet April 20-24, with headquarters at The Conrad Hilton Hotel, Chicago, Dr. Eliot E. Foltz of Winnetka, Ill., general chairman, announced. The presentation will include more than 100 papers, 23 panels, clinics at 13 hospitals, 6 clinical-basic science case conferences, 12 color television clinics, 31 clinical investigation reports, 18 scientific exhibits, and a technical exhibit. In the morning, two-hour clinics will be held in the hospitals, followed by panels in the hotel and in the Blackstone and Eighth Street Theaters. At the same time, clinical-basic science case reports will be held in the hotel. A new feature will be a public meeting to which business, civic, and nonmedical professional leaders will be invited. A panel will discuss "The Care and Preservation of the American Executive." The panelists will be Drs. Philip S. Hench, Henry L. Bockus, William C. Menninger, Chester M. Jones, Sara M. Jordan, Howard P. Lewis, Irvine H. Page, and Walter L. Palmer. Dr. Dwight L. Wilbur, of San Francisco, president of the college, will be moderator. The annual business meeting will be held April 23. Officers, regents, and governors will be elected. Dr. Howard P. Lewis, of Portland, Ore., will be inducted as president to succeed Dr. Wilbur. The annual convocation, will be held the evening of April 22, and will include an address by Dr. Wilbur. For information, write Mr. E. R. Loveland, Executive Director, The American College of Physicians, 4200 Pine St., Philadelphia 4.

International Committee on Aging Problems.—An International committee to exchange with foreign countries information about health and welfare programs for older people was established by the National Committee on the Aging. Chairman of the international committee is Dr. Michael M. Dacso, director, physical medicine and rehabilitation, Goldwater Memorial Hospital, New York City. The committee's first task will be to exchange information and experience with leaders of health and welfare programs for older people in Europe and Asia. The National Committee on the Aging, a standing committee of the National Social Welfare Assembly, is a national resource for planning, information and consultation in the field of aging. It is a nonprofit organization.

FOREIGN

Veterinary Congress in Madrid.—The 16th International Veterinary Congress will be held May 21-27 in Madrid, Spain, at the Faculty of Medicine, University City. Two general subjects are planned: "Social Mission of the Veterinary Science and Practice" and "Nuclear Energy and Veterinary Sciences." Section titles are as follows:

Veterinary Medicine.
Epizootology.
Veterinary Public Health.
Zootechnics.
Veterinary Profession.

A program of films, excursions, receptions, and a ladies' program are planned. The official languages will be Spanish, French, English, and German, and simultaneous translation will be provided. For information write the 16th International Veterinary Congress, 11, Villanueva Street, Madrid, Spain.

Symposium on Bacterial Resistance.—On May 1-3 a symposium on the Prevention of Bacterial Resistance to Antibiotics in Obstetrics and Gynecology will be held in Perugia, Italy, sponsored by the Italian Society of Obsterics and Gynecology. The symposium, to be held at the University of Perugia, will have the following session titles:

Problems Relating to Bacterial Resistance in a Maternity Hospital.
  (a) Resistant organisms in the wards of an obstetrical and gynecological service.

- (b) The problem of bacterial resistance and infections in obstetrics and gynecology.

Suggestions for the Prevention of Bacterial Resistance.

- (a) Extension and limitations in the prophylactic use of antibiotics and chemotherapeutics (operative vaginal deliveries, caesarian sections, infected abortions and labors, gynecological operation, etc.).
- (b) Reserved antibiotics in safe-keeping. Their use in emergency cases.
- (c) Nonantibiotics and analogous drugs as prophylactic and therapeutical agents in infected cases in obstetrics and gynecology.

Conclusions.

No fees are required for registration. Simultaneous interpretations will be provided in Italian and English, and proceedings will be recorded for publication. A ladies' program and entertainment schedule are planned. Correspondence should be addressed to: Segreteria del Simposio, Clinica Ostetrics e Ginecologica dell'Università, Policlinico, Perurgia, Italy.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application was Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application was Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Boston, April 16-19. Final date for filing application was Feb. 28. Sec., Dr. Edward B. Smith, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Preventive Medicine: *Public Health.* Minneapolis, Boston, Baltimore, Chapel Hill, North Carolina and New Orleans, April 9-11; Berkeley, Calif., April 23-25; Pittsburgh, April 16-18. *Occupational Medicine.* Chicago, April 24-26. *Aviation Medicine.* Los Angeles, April 24-26. Final date for filing all applications is March 16. Sec., Dr. Tom F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application is July 1. *Oral.* September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

ARMY

Personal.—Brig. Gen. Perrin H. Long of Brooklyn, N. Y., has transferred to the Retired Reserve. He began his military career in the ranks during World War I. After receiving a direct appointment as lieutenant colonel in August, 1942, he served on active duty in North Africa and Europe as a medical consultant. He completed more than 18 years of active and reserve service; his last assignment prior to retiring was mobilization designee as a special assistant to the Surgeon General.

NAVY

Film Certificate Awarded.—The Navy received an Edinburgh International Film Festival certificate for a Bureau of Medicine and Surgery film entitled "Color Vision Deficiencies." The certificate was presented by British Ambassador Sir Harold Caccia in March. The Edinburgh Festival is an annual event. Over a period of 15 years, the Navy has been given about 34 national and international awards for its motion pictures. "Color Vision Deficiencies" (MN 8246) is a 16-mm. color film with sound. The running time is 20 minutes. It is intended for medical department personnel who are responsible for color vision tests.

Captain Shone Elected.—Capt. Lloyd B. Shone, Medical Corps, U. S. Navy, was elected secretary of the American Academy of Occupational Medicine at the Academy's 11th Annual Meeting in Boston in February. He is presently director of the Occupational Medicine and Dispensary Division in the Bureau of Medicine and Surgery and is certified as a specialist in occupational medicine by the American Board of Preventive Medicine.

VETERANS ADMINISTRATION

Dr. Middleton Reappointed.—Dr. William S. Middleton was reappointed for a second four-year term as chief medical director of the Veterans Administration. As VA chief medical director, he heads the agency's 171 hospitals, nearly 100 outpatient clinics, and nationwide hometown medical services, which together provide care for about 2,500,000 patients yearly.

PUBLIC HEALTH SERVICE

Embryology Committee.—An experimental Embryology and Development Training Committee was appointed by the surgeon general. It held its first meeting at the Harvard Medical School in February. Under the chairmanship of Dr. Louis Bellman, professor and chairman of obstetrics and gynecology at the State University of the New York School of Medicine, the committee will review training grant applications in experimental embryology and related basic sciences. It will function under Dr. G. Halsey Hunt, chief of the division of general medical sciences, and Dr. Frederick L. Stone, assistant division chief and chief of the research training branch. Dr. Howard P. Jenerick will be executive secretary. The work of the committee, which is made up of members representing many of the basic specialties related to human reproduction and development, will help meet the increasing need for emphasis on research training in these fields. The program will support research training for postresidents or other postdoctoral and predoctoral trainees in electron microscopy, genetics, developmental physiology, neonatal pathology, fetal biochemistry, and other related basic science fields. In addition to Dr. Hellman, members of the committee include Drs. Robert A. Aldrich, University of Washington School of Medicine, Seattle; Harry H. Gordan, Sinai Hospital, Baltimore; Duncan E. Reid, Boston Lying-in Hospital, Boston; Howard C. Taylor, Columbia-Presbyterian Medical Center, New York; and James G. Wilson, University of Florida College of Medicine, Gainesville, Fla.

Training in Epidemiology.—A course in applied epidemiology will be offered at the Communicable Disease Center in Atlanta, Ga., May 4-8, 1959, as a part of the continuing program of the center's training branch. This course is designed primarily for physicians who serve as investigators of disease outbreaks or have administrative responsibility for such investigations. It serves both as a refresher course for the experienced health administrators and as an introductory course for physicians new to public health. Emphasis is placed on developing and understanding of how epidemiologic techniques can be used in the approach to the solutions of problems in the preventable disease field. Lecture-discussion sessions and audiovisual aids are used in the presentations, but emphasis is placed on group participation, which is obtained through group solution of epidemiologic problems, seminar-type presentations, and panel discussions. Registrants will be expected to attend all sessions of the course. Further information and application forms may be obtained from: Chief, Communicable Disease Center, Public Health Service, 50 Seventh St. N. E., Atlanta 23, Ga., Attention: Chief, Training Branch.

DEATHS

Owen, Abraham Miconias Ⓜ Bloomington, Ind.; Indiana University School of Medicine, Indianapolis, 1940; veteran of World War II; associated with Bloomington Hospital; died Jan. 12, aged 58.

Pennell, Samuel, Brooklyn; Cornell University Medical College, New York City, 1926; veteran of World War II; on the staffs of the Jewish and Maimonides hospitals; specialist certified by the American Board of Pathology; died Jan. 1, aged 58.

Potter, Joseph Lumbard Ⓜ Duke Center, Pa.; Medico-Chirurgical College of Philadelphia, 1916; died Dec. 22, aged 65.

Rogers, Charles Lewis Ⓜ Norman, Okla. (licensed in Oklahoma by years of practice); died in a hospital at Bartlesville Jan. 26, aged 82.

Rose, Joseph Everett Ⓜ Pensacola, Fla.; University of Alabama School of Medicine, Mobile, 1909; died Dec. 28, aged 79.

Scott, James Stanley, Pomona, Calif.; University Medical College of Kansas City, Mo., 1896; died Dec. 17, aged 92.

Shipper, Philip Marvin, New York City; Indiana University School of Medicine, Indianapolis, 1934; served on the staffs of the Cornell Medical Center–New York Hospital and Beth David Hospital; died in the New Rochelle (N. Y.) Hospital Dec. 24, aged 48.

Siminson, Irwin Dave Ⓜ Mineral Point, Wis.; Rush Medical College, Chicago, 1924; for many years practiced in Chicago, where he was on the staff of the Mercy Hospital and chief surgeon with the New York Central Railroad; died Jan. 26, aged 63.

Skinner, James Edwards, Tacoma, Wash.; Rush Medical College, Chicago, 1896; for many years a medical missionary in China; died in Battle Ground Jan. 12, aged 91.

Sonnenschein, Joseph Benjamin Ⓜ Chicago; Rush Medical College, Chicago, 1902; veteran of World War I; for many years connected with the city board of health; died in the Chicago Wesley Memorial Hospital Jan. 30, aged 82.

Stalker, John Morton, Borden, Ind.; University of Louisville (Ky.) Medical Department, 1906; served as trustee of the Borden Schools; on Thanksgiving Day in 1957 Borden proclaimed "Dr. Stalker Day" at the Borden High School; died Jan. 10, aged 76.

Staples, Mary Morrison, San Francisco; University of California School of Medicine, San Francisco, 1894; died Jan. 14, aged 98.

Stapp, Roth Van Allen, Houston, Texas; St. Louis University School of Medicine, 1930; veteran of World War II; died Jan. 19, aged 53.

Stevenson, Holland Newton Ⓜ Pelham, N. Y.; born in Pittsfield, Mass., in 1886; Johns Hopkins University School of Medicine, Baltimore, 1912; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; formerly on the faculty of his alma mater, Columbia University College of Physicians and Surgeons in New York City, Creighton University School of Medicine in Omaha and at the New York Post-Graduate Medical School and Hospital in New York City; associated with the New Rochelle (N. Y.) Hospital; a director of the National Bank of Westchester; died Jan. 11, aged 72.

Swart, William Sheridan Ⓜ Girard, Kan.; Barnes Medical College, St. Louis, 1899; died Dec. 19, aged 83.

Swenson, Henning Melville Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1929; veteran of World War I; on the staff of the Augustana Hospital for many years; died Jan. 17, aged 58.

Taubenhaus, Matthew Ⓜ Chicago; born in Warsaw, Poland, Nov. 29, 1903; Medizinische Fakultät der Universität, Vienna, Austria, 1928; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Endocrine Society, Chicago Society of Internal Medicine, Society of Experimental Biology and Medicine, American Diabetes Association, New York Academy of Sciences, and the American Association for the Advancement of Science; in 1952 a Claude Bernard visiting professor at the University of Montreal; in March, 1939, came to the United States and began his association with Michael Reese Hospital; first in the department of metabolic and endocrine research and then in the department of medicine; at the time of his death, was attending physician at the hospital and vice-chairman of the department of medicine; died Jan. 16, aged 55.

Ⓜ Indicates Member of the American Medical Association.

Traweek, Albert Carroll Sr. Ⓜ Matador, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1901; member of the American Academy of General Practice; for many years county health officer; superintendent of the Traweek Hospital, of which he was the owner; died in the Quanah (Texas) Memorial Hospital Jan. 10, aged 83.

Troncoso, Manuel Uribe Ⓜ New York City; born June 17, 1867; Universidad Nacional Facultad de Medicina Mexico, D. F., 1890; specialist certified by the American Board of Ophthalmology; served as professor of ophthalmology at the New York Post-Graduate Medical School and Hospital and assistant professor of clinical ophthalmology at the Columbia University College of Physicians and Surgeons; in 1942 received the research medal of the American Medical Association Section on Ophthalmology; author of "A Treatise on Gonioscopy"; wrote "Internal Diseases of the Eye and Atlas of Ophthalmoscopy," which has gone through many editions; died in the Frances Schervier Home and Hospital Jan. 21, aged 91.

Underwood, Felix Joel Ⓜ Jackson, Miss.; born in Nettleton, Nov. 21, 1882; Memphis (Tenn.) Hospital Medical College, 1908; began his public health career in 1918 as health officer for Monroe County and served until 1921; in the latter year came to Jackson and became director of the Bureau of Child Hygiene for the Mississippi State Board of Health, serving until 1924, when he became executive officer and secretary and held that post until his retirement in June, 1958; served as president of the American Public Health Association; twice was the recipient of the Lasker Award; received it first in 1945 for his planned parenthood program, and again in 1953 for outstanding public health administration; in 1941 president of the Southern Branch of the American Public Health Association and served as chairman of the regional executive board and member of the governing council; past-president of the Southern Medical Association, Mississippi Public Health Association, Conference of State and Provincial Health Authorities of North America, Mississippi State Medical Association, State Conference of Social Work, and the State Board of Examiners for Nurses; from 1912 to 1925 secretary of the Northern Mississippi Thirteen Counties Medical Society; director at large, National Tuberculosis Association from 1942 to 1944; served as a member of the board of directors of the American Cancer Society and recipient of a plaque as an award for meritorious service as campaigning chairman for the state division in 1948; member of the House of Delegates of the American Medical Association from 1933 to 1946 and from 1949 to 1951; general chairman of the Mississippi Council for Child Health and Protection; member of the State Board of Public Welfare from 1933 to 1935; delegate to several congresses and conferences; specialist certified by the American Board of Preventive Medicine, of which he served as vice-chairman; associate in public health, University of Mississippi School of Medicine; guest lecturer, Tulane University in New Orleans and Meharry Medical College in Nashville, Tenn.; special consultant to the surgeon general, U. S. Public Health Service, and to the National Advisory Mental Health Council; fellow of the American College of Physicians; for three years served as a member of the board of scientific directors of the Rockefeller Foundation in New York City; for many years member of the board of directors of the Standard Life Insurance Company; member of the staffs of the Mississippi Baptist, St. Dominic, and Mississippi State Charity hospitals; secretary of the board of trustees of the Mississippi State Tuberculosis Sanatorium; member of the state commission on hospital care; member and past-president of the board of trustees of the Mississippi Children's Home Society; for many years state fund raising chairman of the National Foundation for Infantile Paralysis; also served in an executive capacity for numerous other community and health organizations; a state building was named in his honor; in 1950 received the Arthur T. McCormack Award; in the last three weeks of his life, received two top accolades for service to his state; United Press International newspaper, TV, and radio editors named him "1958 Man of the Year"; winner of the new University of Mississippi–First Federal Foundation "Missy" award for distinguished service; the *Mississippi Doctor* for September, 1944, was designated the Underwood issue in his honor; the journal carried many tributes for him and a review of the health of the state under his direction; joint author of "History of Public Health and Medical Licensure," Vol. I, 1798-1937, Vol. II, 1938-1947; died Jan. 9, aged 76.

Vander Veer, Albert Ⓜ Charlotte, N. C.; Columbia University College of Physicians and Surgeons, New York City, 1904; specialist certified by the American Board of Internal Medicine; practiced in New York City for many years and was associated with the Roosevelt Hospital; veteran of World War I; past-president of the American Academy of Allergy; died in the Presbyterian Hospital Jan. 31, aged 79.

Vorpahl, Rudolph Augustus Ⓜ Cedar Rapids, Iowa; Milwaukee Medical College, 1905; veteran of World War I; for many years county coroner; died Jan. 14, aged 78.

FOREIGN LETTERS

AUSTRIA

Icterus Neonatorum.—At the meeting of the Society of Physicians in Vienna on Jan. 30, Dr. H. Gross stated that the most important form of icterus in the newborn infant is the icterus gravis associated with erythroblastosis fetalis. Patients with this type of icterus must be given exchange blood transfusions to prevent early death or permanent damage because of kernicterus resulting from hyperbilirubinemia. Other diseases to be considered in the differential diagnosis include epidemic hepatitis; the rare homologous serum hepatitis; congenital cirrhosis of the liver; acute yellow atrophy; occlusion of bile ducts by aplasia, artresia, stenosis due to choledochus cysts or adhesions, or thickened bile; general sepsis; congenital syphilis; toxoplasmosis; cytomegaly; listeriosis; occasionally diabetes mellitus, a prediabetic condition of the mother or a toxemia of pregnancy; and rarely cystic fibrosis of the pancreas. Administration of large doses of vitamin K may also lead to hyperbilirubinemia. One may observe a prolonged icterus also in children with congenital thyroid deficiency. In addition a severe, long-continued icterus frequently occurs in premature infants and is due to a functional immaturity of the liver. Exchange blood transfusions may be considered for the prevention of kernicterus in patients with a rise of the indirect bilirubin serum level to more than 20 mg. per 100 cc.

Pheochromocytoma.—At the meeting of the Society of Physicians in Vienna, on Jan. 6, Drs. O. Kraupp and H. Bernheimer stated that a greatly increased excretion of pyrocatechin is pathognomonic of a pheochromocytoma. A slightly increased renal excretion of epinephrine does not, however, rule out the presence of a chromaffin tumor. The speakers confirmed the diagnostic significance of the 3-methoxy-4-hydroxymandelic acid excreted in the urine of a patient with a tumor secreting levarterenol and epinephrine. The symptoms disappeared and the amount of pyrocatechin excretion, which was high in the beginning of observation, dropped within a few weeks; but the 24-hour excretion of the mandelic acid derivative remained high and assured the diagnosis of pheochromocytoma. In this case the *p*- and m-hydroxyhippuric acid excretion was also greatly increased. After excision of the tumor the excretion of the abovementioned acids decreased to normal. The speakers hoped that by determining the renal excretion of the decomposition products of pyrocatechin the differential diagnosis of a suspected chromaffin tumor would be improved.

BRAZIL

Postoperative Sodium and Potassium Metabolism.—Dr. J. de Moraes and co-workers, of the Rio de Janeiro Hospital São Miguel, (*Rev. brasil. cir.* 36:137, 1958) studied the metabolism of sodium and potassium in 20 patients, 18 of whom had had gastrointestinal operations and 2 of whom had had operations on the respiratory tract. Water, sodium chloride, and potassium balance studies were made on all patients for eight days, as well as determinations of electrolytes in the plasma on the first, third, and fifth postoperative days. The authors concluded that in the immediate postoperative period there is a low output of sodium in the urine with paradoxical low level of plasma sodium. In this period sodium must be given carefully and the extrarenal salt loss through vomiting, fistulas, and gastric and jejunal aspiration should be compensated in accordance with the amount lost.

When the urinary sodium retention and the hyponatremia last for more than eight days, in spite of adequate replacement, operative complications should be looked for and treated, instead of concentrating on the hyponatremia. An increased output of urinary potassium in the immediate postoperative period and discreet hypopotassemia during the third and fifth postoperative days were observed. This increase in potassium excretion is due in part to the adrenergic corticoid phase. In patients who have taken nothing by mouth for five or more days there may be a depletion of potassium with evident symptoms, abnormalities in the electrocardiogram, and, less frequently, hypopotassemia. If a long period of no oral intake is foreseen, the administration of potassium should be started from the first day, to avoid depletion. In dehydrated patients the potassium replacement must be preceded by rehydration to insure a good output of urine.

Cyanosis in Schistosomiasis.—Dr. J. V. Barbas and co-workers, at a meeting of the Associação Paulista de Medicina reported a case of hepatosplenic schistosomiasis due to Schistosoma mansoni in which the patient showed, during the last part of his illness, dyspnea on exertion and an intense and progressive cyanosis. Physical examination of the lungs, roentgenograms of the chest, and an electrocardiogram

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The items in these letters are contributed by regular correspondents in the various foreign countries.

showed no abnormalities. Functional tests of the lungs suggested the presence of a pulmonary arteriovenous fistula. This was confirmed by angiocardiography. Cardiac catheterization showed normal pressure in the pulmonary artery and an increased cardiac output. The pulmonary biopsy specimen showed the presence of schistosomes and of several fistulas between the small branches of the pulmonary artery and the pulmonary veins. These fistulas were caused, as demonstrated in a previous investigation by one of the authors, by schistosome ova. The dyspnea and cyanosis were caused by these arteriovenous microfistulas. The authors believed this to be the first reported case of pulmonary schistosomiasis in which, in the absence of cor pulmonale diagnosed during the life of the patient, marked cyanosis was present in addition to the usual symptoms of hepatosplenic schistosomiasis.

Blastomycosis.—Dr. R. M. Castro and co-workers of the São Paulo State University Hospital (*Rev. paulista med.* 53:479, 1958) drew attention to the great difficulties of the diagnosis in some patients with Brazilian blastomycosis and illustrated the problem with the report of eight typical cases. As a rule, this disease does not present diagnostic difficulties, as its two common forms—the mucocutaneous and the lymphaticovisceral—present pathognomonic signs and their lesions abound in Blastomyces brasiliensis. Difficulties arise, however, when the process remains restricted to the lymph nodes without a tendency to softening and fistulization or because localized in deep organs without tegumentary manifestation, or when the tegumentary lesion is so small that it escapes discovery. Without the demonstration of the parasite, and the lesions clearly simulating those of other diseases, the diagnosis is sometimes difficult. Of the eight cases presenting diagnostic difficulties two resembled Hodgkin's disease and the diagnosis was established only after lymph node biopsy; three which could be classified as an icteric form had a bout of obstructive jaundice caused by compression of the biliary ducts by masses of enlarged lymph nodes and the diagnosis was made at operation; one simulating a severe hemopathy was diagnosed only at autopsy; one died before a diagnosis could be made and was diagnosed at autopsy; and one simulating adrenocortical hypofunction also could be diagnosed only at autopsy.

An early and accurate diagnosis is of the utmost importance because specific treatment can now cure what is otherwise a highly fatal disease. Aside from identification of the causative organism, laboratory tests are of little value. Hyperglobulinemia, however, suggests a granulomatous process. This may give a valuable clue in cases simulating a neoplastic or leukemic process, since in those conditions hyperglobulinemia does not occur.

FINLAND

The Training of Specialists.—Last summer representatives of the Scandinavian Medical Associations met in Ulvik to discuss, among other things, postgraduate study and the training of specialists. Dr. Kosonen, of Finland, pointed out that before 1932 no organization had had authority to confer on physicians the title of specialist. Since then the committee created by the Finnish Medical Association for this purpose has issued rules which have needed revision from time to time so as to reflect the most recent experiences in this sphere. By now there are 37 fields in which a physician may qualify as a specialist, but there are only 14 main specialties. Broadly speaking, the specialist must have a year of ordinary postgraduate training plus three years of some special subject studied at a teaching hospital. Hitherto he has not been required to pass any special examination on his specialty, and his qualifications have not been scrutinized by any disciplinary body. Of late there has been a controversy over the creation of a new board of examiners of candidates for the title of specialist, with the public health authorities, the medical faculties, and the Finnish Medical Association pulling in different directions. Dr. Kosonen would like to see the standards of specialty training in Finland brought closer to the level of the other Scandinavian countries. For the present this would require study in medical centers outside Finland.

Pediatric Surgery.—Dr. M. Sulamaa, of the Helsinki Childrens Clinic, recommended that operations on children be performed in a children's rather than a general hospital (*Nordisk medicin,* Dec. 18, 1958). His study for the period 1947 to 1957 includes a wide range of cases which he classes as general, septic, urologic, thoracic, orthopedic, or neurological surgery and tumors. In each of these spheres he would like to see the development of pediatric surgery always within the framework of a children's hospital. Even the surgical instruments of a children's hospital are distinctive, witness the special characteristics of the outfit for intravenous injections. There are also special requirements for the feeding and washing of children, all much different from the corresponding requirements for adults.

Conditions in Lapland.—In 1956 a series of field studies of intestinal infections in a part of Finnish Lapland with a population of about 5,500 was made. Aided by the Department of Epidemiology of the Harvard School of Public Health, this team issued a report (*Nordisk medicin,* Jan. 22, 1959) which gives an illuminating picture of social conditions peculiar to this part of Finland. The ravages of World War II were so great that practically all the houses in the area in question were new. These houses, built since 1944, provide an anteroom or even two such rooms in succession so as to keep the main living room comparatively warm. A living room opening directly onto the outer world is now rare. Owing to great distances from school, many children have to live in boarding houses during the school term. Milk is not pasteurized and it passes from the producer direct to the consumer in most cases. When there is an intermediate agent, care is taken to keep the various supplies separate to avoid wholesale mixing. The slaughtering of reindeer is limited to the winter when the meat is kept frozen by natural means. Meat required for consumption in the summer is lightly salted and then smoked and dried in the winter. Here, again, the middleman is usually avoided, the householder either producing his own meat or getting it from his neighbor. Fresh meat is not eaten in the summer when fish becomes the householder's staple diet, much enriched toward the end of the summer by fruit and vegetables. Thanks in large part to the customary weekly steam bath, the personal cleanliness of this community is noteworthy.

INDIA

Alcaligenes Faecalis.—Sarkar and Tribedi (*Indian Journal of Medical Sciences*, vol. 12, December, 1958) stated that Alcaligenes faecalis, although described as a normal inhabitant of the intestinal tract, has also been reported by many workers to be the cause of enteric-like fever, meningitis, cystitis, abscesses, appendicitis, arthritis, and other conditions. For this reason all the strains of A. faecalis isolated from pathological material (blood, urine, feces, pus, and spinal fluid) received from different wards were studied by the authors. The feces of normal healthy persons and the feces of patients convalescing from acute diarrhea, dysentery, cholera, and typhoid were also cultured. All the strains were grown in special mediums to distinguish soil-forms of this organism from the intestinal type. Swabs from hands of house staffs and nurses and from the skin of the antecubital fossae of patients with a blood culture positive for A. faecalis were also cultured. Animal pathogenicity tests were made by injecting guinea pigs, rabbits, and mice by different routes with this organism, with or without mucin.

Previous immunization had been accomplished in some cases. Antibody response in patients from whose blood the organism was isolated was also found, blood from normal persons being used as a control. Of 1,960 consecutive blood cultures in a period of three years, A. faecalis was isolated from 93 patients, in 71 of whom the symptoms resembled those of typhoid, and in 14, atypical typhoid with remittent or intermittent fever. Two patients had puerperal fever, two had high fever late in pregnancy, one had fever following abortion, and three had subacute bacterial endocarditis. A. faecalis was isolated from 58 urine samples showing albumin and pus. During the period of study three patients had meningitis, two had abscess, one had pericardial effusion, one had pleural effusion, and one had cervicitis, all yielding A. faecalis on culture. The agglutinin titer could be determined in 32 patients with enteric-like fever whose blood cultures were positive for A. faecalis. Results of the Widal tests were negative in 9; the titer varied from 1:50 to 1:1,250 in 10; and in 13 it was below 1:50. The culture of swabs from the hands of nurses and house staff was uniformly negative, as were the cultures from the skin of antecubital fossae.

A. faecalis was isolated from 2 of 60 stools from healthy persons, 6 of 30 stools from patients convalescing from typhoid, 4 of 12 convalescing from dysentery, and 30 of 120 convalescing from cholera. By growing the strains in the synthetic mediums most of them could be identified as of fecal rather than soil origin. Animal pathogenicity tests showed the organism to be definitely pathogenic in mice when injected with mucin. When injected in an isolated intestinal loop of a rabbit, many strains were revealed to be pathogenic. In none of the patients in this series could a second organism be isolated from any pathological material. Immunizing injections produced protective antibodies in mice, supporting the pathogenic nature of this organism. All the strains, however, are not pathogenic and the virulence is not high. A high agglutinin titer is not a prominent feature of this infection, although 23 of the 32 patients so tested showed an antibody response. The organism could be isolated from the stools of only 2 of the 60 normal subjects, thus throwing doubt on its status as a normal intestinal inhabitant. Its incidence was, however, found to increase in intestinal disorders such as dysentery, acute diarrhea, and cholera. Most of the reported infections with A. faecalis have been from the tropics and subtropics. The authors believe that it probably plays a pathogenic role in these places and, when isolated from pathological material, should be considered as such and not just dismissed as a contaminant.

Gastroenteritis in Children.—Manchanda and Arora (*Indian Journal of Paediatrics*, vol. 25, November, 1958) analyzed a series of 665 cases of acute diarrhea in young children with regard to cause. Of 4,438 patients admitted during the two and one-half year period of study 665 (15%) had acute diarrhea. Of these 77.4% were in the first year of life. In this series 109 (16.4%) died, of whom 79 (15.3%) were below the age of 1 year. More than half the cases developed in the summer months. The mortality among bottle-fed infants was 21.3% compared to 9.18% among breast-fed babies; 424 patients came from poorer families with unsatisfactory housing conditions. Evidence of infection was present at the time of admission in 140 patients—66 had tonsillitis and pharyngitis, 30 had acute upper respiratory infections, 15 had a discharging ear, 14 had bronchopneumonia, 8 had multiple boils, and 7 had blepharitis. A history of previous attacks of gastroenteritis was obtained in 109, and a history of acute episodes of diarrhea in other siblings in the family was obtained in 72 cases. Stools were examined bacteriologically in only 50 cases. Serologic types of Escherichia coli 055 and 0111 were present in 30% of the specimens. A total of 84 strains were isolated from the stool specimens studied. Besides Esch. coli, other bacteria isolated were Paracolobactrum coliforme, 31.6%; Staphylococcus pyogenes var. aureus, 21.6%; Pseudomonas aeruginosa, 13.3%; and Shigella flexneri, 1.2%. In most stools more than one organism was isolated, pure growth of a single organism being found only rarely.

The incidence of toxemia, severity of the disease, and mortality rates were higher in patients excreting Proteus vulgaris, Ps. aeruginosa, and Staph. pyogenes var. aureus. Thus the mortality from Ps. aeruginosa infection was 66.7%; that from P. vulgaris infection was 37.5%; and that from Staph. pyogenes var. aureus infection was 26%. Esch. coli 0111 was found in three patients under the age of three months (one died), in two between the ages of three and six months, and in one over six months. Esch. coli 055 was isolated in six patients under the age of three months (one died) and in five between three and six months (one died).

All 665 patients were admitted as emergencies, having proved refractory to treatment outside; 384 had vomiting, 93 had blood and mucus in the stools, and dehydration of varying degrees was present in 505. Fluids were given intravenously to 490 and subcutaneously aided by hyaluronidase in 15. These fluids included dextrose solution, plasma, and whole blood. Saline solution was given if vomiting was excessive. Potassium chloride or citrate was added when dehydration was sufficiently overcome and the child started passing urine. Some patients also received calcium gluconate and multivitamin preparations parenterally. Various drugs such as sulfaguanidine, sulfasuccidine, streptomycin, chloramphenicol, chlortetracycline, and various combinations of antibiotics were given.

Blood Histamine in Adults.—Basu and Bhattacharya (*Indian Journal of Medical Sciences*, vol. 12, December, 1958) stated that in certain diseases, histamine is believed to be endogenously liberated, leading to variations in the blood level. It is therefore necessary to know the normal range of blood histamine before such pathological conditions can be distinguished from the normal variations. The authors estimated the blood histamine level of 25 healthy adults, excluding anyone with a history of cutaneous, nasal, or respiratory allergy. Estimations of hemoglobin concentration, total erythrocytes, and total leukocytes, and the absolute eosinophil count were also made. The normal range of blood histamine was found to vary from 1.0 to 6.2 mcg. per 100 ml. of whole blood, with a mean value of 3.8. The absolute eosinophil count ranged from 50 to 450 per cubic millimeter. There was no correlation between the blood histamine level and the absolute eosinophil count. These figures resembled those obtained by workers in other countries, although the highest range observed here is a little lower than that obtained by others.

Expansion of Health Services.—An indication of the standard of national health before India achieved independence could be estimated from the life expectancy of men and women, which was 26.9 years and 26.6 years, respectively, for the decade ending in 1930 and 32.5 and 31.7 years for the decade ending in 1950. Lack of medical facilities, technical personnel, and water supply were among the factors that contributed to this state of affairs. Inadequate financial resources further aggravated the situation. The first Five Year Plan allotted priorities to rebuilding the nation's health and laid the foundation for further progress. The Second Plan envisages bringing health services within the reach of all people. The specific objectives under the Second Plan are establishment of institutional facilities to serve as bases from which health services can be extended, training of technical manpower, control of communicable diseases, campaign for environmental sanitation, and family planning.

Surgical Treatment of Tuberculosis.—Padhi and Lynn (*Indian Journal of Tuberculosis*, vol. 6, December, 1958) reported that such procedures as phrenic paralysis, pneumothorax, and pneumoperitoneum have fallen into disuse in the treatment of pulmonary tuberculosis, their place now being taken by resection. Not a single pneumothorax or pneumoperitoneum was induced in their hospital in the last three years. In the authors' series of 150 pulmonary resections the indications were absolute in 118 and relative in 32; 41 had residual cavities, 38 had residual caseonodular lesions, 36 had destroyed lobes, 24 had destroyed lungs, 8 had tuberculoma or inspissated cavities, and 3 had bronchopleural fistula. Of those with residual caseonodular lesions 32 were subjected to resection as a prophylactic measure against reactivation, as they lived far away from the sanatorium and were likely to be lost to follow-up examinations over long periods. Advanced age was not considered a contraindication if the cardiorespiratory reserve was satisfactory. Thus, 15 patients in this series were 50 to 59 years of age and two were over 60; 16 had extremely poor pulmonary function. They were persistently positive, drug-resistant, and had undergone prolonged sanatorium treatment. The morbidity and mortality in these resections was high, but the risk of operation was preferable to a long downhill course. Of these 16 patients 3 died, but 13 were rehabilitated. Most of the 150 patients were between 20 and 30 years of age. All had had initial sanatorium treatment with chemotherapy which varied from three months to several years. On admission 139 had positive sputum; 46 had positive sputum and were drug-resistant at the time of resection. Bronchoscopy was performed routinely prior to operation to exclude endobronchial disease; bronchography was done in most of these cases. Deep breathing exercises and diaphragm control were started one week before operation and continued postoperatively.

SWEDEN

Treatment of Psychiatric Patients with Iproniazid.—Norring and Gottfries (*Svenska Läkartidningen*, Jan. 9, 1959) treated 100 patients at the psychiatric department of a general hospital in Malmö with iproniazid. The main indications for this treatment were depressive and asthenic states and the initial dosage was 25 mg. three times a day for a week, after which it was sometimes cautiously raised. The maximum reached was 150 mg. daily. The duration of treatment was up to seven months. In many patients the results were surprisingly good, but there were also many undesirable side-effects leading to withdrawal of the drug within a fortnight in 6 patients and after a longer interval in 17. In 58 patients hypotonic disturbances manifested themselves in giddiness, faintness, tinnitus, and "blackness of vision." Those with already existing hypotonia were much embarrassed by these hypotonic disturbances. Other side-effects were profuse sweating, headache, edema, and stranguria which in two of eight patients required catheterization that had to be continued two days after the drug had been withdrawn. There were also mental disturbances such as hypomania, which was observed in five patients.

Many of the 100 patients had been refractory to other methods of treatment such as electroshock, insulin, and sedatives, so the numerous successes achieved by iproniazid were the more impressive and an incentive to further trial under the closest control of the blood pressure, urine, and body weight. Hypertonic patients and others with a history of liver or kidney disease needed specially close watching. Epilepsy should be regarded as a contraindication for this treatment. The drug gave disappointing results in patients with presenile depressive states.

Cholesterol Metabolism.—Dr. H. Malmros of the University Hospital at Lund (*Nordisk medicin*, Jan. 2, 1959) reported on experiments carried out at his hospital by Dr. G. Wigand who fed rabbits a semisynthetic diet of pellets containing sugar, starch, casein, vitamins, 8% coconut fat, and salts, but no cholesterol. In spite of the total lack of cholesterol in this diet, the rabbits developed marked hypercholesteremia after a few weeks. On the completion of these tests after 110 days, atheromatous changes were plainly demonstrable in the aorta. On the other hand, rabbits fed on corn oil presented normal blood vessels. A series of 30 patients suffering from essential, familial hypercholesteremia were treated during the past two or three years by Malmros as follows: Animal fats in the form of butter, cream, milk, cheese, eggs, and meat fats and such other fats as margarine and cocoa fat were excluded from the diet, and dried milk and cheese from which milk fats had been abstracted and corn oil were substituted. This oil was used for salad dressing, mixed with porridge and mashed potatoes, and used for frying. Vegetables, fruit, sugar, and cereals were permitted, but bread made of wheat and cakes made with butter were omitted. Later fish, even fat fish, was added. Most of the 30 have been on this diet for over a year and they have on the whole tolerated it well. This diet was regularly followed in a couple of weeks by a fall in the serum cholesterol level. In some subjects there was a further fall, and in others the cholesterol maintained a steady level. Further investigations should show whether it is possible by using an appropriate diet to control arteriosclerosis.

When to Prevent Tetanus.—*Svenska Läkartidningen* for Jan. 16 again published (without giving the names of the offenders) cases brought to the attention of the Swedish Doctors' Disciplinary Committee. This time the hardy perennial question was raised: When should a wound be treated to prevent tetanus? A man, aged 63, injured his left index finger in a carding machine on Nov. 10, 1956. The terminal phalanx was amputated at a surgical polyclinic where bruised tissues were removed and the wound dressed. No prophylactic injection of tetanus serum was given but he was given penicillin at that time and again on his return to the clinic on Nov. 12 and 14. On Nov. 21 he returned complaining of severe pain in the finger and some necrotic tissue was removed. On the next day he complained of pain and stiffness in the nape of his neck and jaws. Tetanus being suspected, he was admitted to hospital whence he was discharged on Dec. 10 after having undergone a relatively mild attack of tetanus. While refusing to censure the doctors concerned, the committee took the occasion to quote the opinion voiced by the Swedish Surgical Society in 1951 to the effect that antitetanic serum should not be given merely for safety's sake but solely for real indications. The fact remains that 30 or more cases of tetanus continue to occur every year in Sweden, and the committee quoted the opinion of one of its experts that it would be well for the nation as a whole to be given the triple vaccine (whooping cough, diphtheria, and tetanus) soon after birth.

CORRESPONDENCE

PHYSICAL FITNESS OF YOUTH

To the Editor:—The paper by Lane on "The Role of the Pediatrician in Physical Fitness of Youth" in The Journal (169:421-427 [Jan. 31] 1959) should not remain unchallenged. The American Medical Association has repeatedly called the attention of its members to the fallacy of accepting the norms for physical fitness on the basis of pure muscle strength. It is the well-recognized duty of every physician who treats children to strive for maximum achievement in all spheres of the young patient's development, and the pediatrician today is making a conscientious effort to guide parents toward that goal. He is appreciative of the fact that not all people are born to be athletes or weight lifters. The pediatrician takes more pride in a cardiac child, who as a youth can consider himself physically fit to be gainfully employed, than in a youngster who achieves stature as the captain of a football team.

"As we look about us today," the author states, "mindful of how seriously we took our responsibilities, many of us find cause for more amazement than pride in some of the children we remember as our healthy infant patients. Too often we see deterioration instead of development; young bodies, once firm and flexible, beginning to go slack and soft. We hear about too many backaches and we are appalled." What does the author mean by deterioration? If the implication is "slack and soft," how tight and hard should a muscle be before it is judged physically fit—and fit for what? Also, I am not aware of the great prevalence of backache as a disease of youth, and I have found quite a number of pediatricians who share this opinion. Not a single one seemed appalled by its incidence.

Is a youth to be considered physically unfit if he is too light for a football club or too short for a basketball team? It is the rehabilitationists who have taught us most about the importance of muscle function rather than mass as a criterion for fitness. One of the best pediatric residents we have had recently was a paralytic. He jumped around on crutches, always ready to learn and to serve. The patients loved him, so did the staff. I considered him physically fit, as did everyone who knew him.

At its annual meeting in 1957 the Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association passed a resolution, part of which follows: "The Joint Committee . . . wishes to reiterate its belief that fitness is not a narrow or limited concept relating, for example, only to physical development, nor is it testable only by muscular strength, agility, or flexibility tests. On the contrary, fitness can be judged only through the use of a battery of evaluative procedures including appraisal of all aspects of organic, psychological, and social growth."

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RADIATION THERAPY AND LEUKEMIA

To the Editor:—The diagnostic problem in The Journal (169:136-142 [Jan. 10] 1959) is an excellent presentation, and the conclusion reached by the authors seems reasonable and correct. The data from which these conclusions are reached, however, are inadequate—particularly the statement that the development of leukemia was the result of radiation therapy, which in one place was said to be intensive and in another place was simply mentioned as having been given. If radiation therapy is to blame for the development of this leukemia, it would seem logical that data be presented concerning the amounts of radiation given, areas treated, duration of time during which these treatments were administered, physical factors of the equipment used, and other necessary information so that one might arrive at a valid conclusion that excessive radiation therapy did lead to the end-result. Such loose reporting as appears in this article has been common in the literature in the past few years and has done more to harm the practice of radiology than has any other factor in the past few decades.

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The above comment was referred to the authors of the diagnostic problem, and they have submitted the following reply.

To the Editor:—In view of Dr. Tainter's perfectly justified criticism we would like to submit the following addendum to the diagnostic problem "Erythremia (Polycythemia Vera), Radiation Therapy, and Leukemia."

The x-ray therapy given the patient, at another institution, is detailed as follows: From Sept. 9 to Oct. 10, 1952, a field 100 centimeters square was used to treat the spleen. A total of 750 r (air) was given in nine divided doses, eight from an anterior port and one from a posterior port. From Oct. 23 to

Nov. 6, 1952, an anterior port was used to treat the tibia and fibula, bilateral, entire length, giving 50 r (air) six times, making a total of 300 r (air). An anterior port was used to treat the femora, bilateral, entire length, giving 50 r (air) six times, making a total of 300 r (air). An anterior port was used to treat the upper extremities, giving 50 r (air) six times, making a total of 300 r (air). Factors in treatment of the spleen and extremities are 200 kv., 50-cm. distance from skin to focus, and half value layer of 0.95 mm. of copper. Triethylene melamine therapy was given from May 29, 1953, to Dec. 20, 1956, intermittently in small doses in courses varying from 1 to 13 weeks, in a total dosage of 260 mg.

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FREEDOM FOR THE PROFESSION

To the Editor:—William S. McCann states in his letter to the editor in The Journal (169:410 [Jan. 24] 1959) that the changes in the treatment of physicians in the German democratic republic are due to "the strength of a strong professional organization." The fact is that no professional organization of any kind exists here and the changes mentioned in the letter were effected after a study by the central committee of the United Socialistic Party (S. E. D.).

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IATROGENIC

To the Editor:—The word iatrogenic was coined several years ago to denote any disease induced by medical treatment. The classic example is cardiac neurosis in a patient whose doctor is too fussy. As such, iatrogenic is probably a useful word, but it is beginning to suffer from misapplication. A good example is the title "Iatrogenic Stiff Shoulders," appearing in the Feb. 28 issue of The Journal, page 945. These stiff shoulders are not produced by the physician, they are produced by the injury and the lack of exercise afterward. To call such a shoulder iatrogenic is akin to calling an embolic death iatrogenic because the doctor did not tie the femoral vein! There might be other factors, too. I think that we should bury the word iatrogenic.

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MISCELLANY

A BACKGROUND PAPER ON KREBIOZEN

American Cancer Society

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I. The Controversy Over Krebiozen

During the past seven years the owners and proponents of Krebiozen, a substance alleged to be beneficial in the treatment of cancer, have been engaged in a great campaign to publicize this substance. They have been disseminating propaganda through articles strategically placed in newspapers, magazines, and books, as well as by organized letter writing, and they have been using national political channels to further their interests. They have already been involved in legislative investigations in two states, California and Illinois.

According to Herbert Bailey's book, "A Matter of Life or Death" (New York, G. P. Putnam's Sons, 1958), these individuals have made it clear that they wish to recoup from the sale of the substance an investment claimed to be about 2 million dollars and that they intend to sell the substance for profit as a proprietary drug. Despite this fact they have repeatedly petitioned health organizations supported by public funds to underwrite a test of the therapeutic efficacy of Krebiozen in collaboration with them. They have hoped to use public funds to defray the cost, estimated at $500,000 or more, of testing this privately owned substance.

Moreover, the chemical composition of Krebiozen remains unknown. The recent claims of its therapeutic efficacy which they have broadcast are based on case histories of patients treated with Krebiozen, although they have not given independent investigators access to these records within the last five years. The owners and proponents have demanded that the substance be tested according to their own terms, which are demonstrably unscientific.

Their steady campaign of publicity ostensibly designed to obtain support from either the American Cancer Society or the National Cancer Institute for testing the substance on their own terms has

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News release of the American Cancer Society dated March 9, 1959.

aroused public interest in Krebiozen. The following documentation which chronicles the history of Krebiozen will provide answers to some of the questions which the public has been asking about this unproved substance.

II. What Is Krebiozen?

Krebiozen is a coined name applied to an alleged anticancer drug. It is said to have been produced by Dr. Stevan Durovic in Argentina prior to 1949. Dr. Durovic claims that he injected 2,000 Argentinian horses with Actinomyces bovis, a microorganism which causes "lumpy jaw" in cattle, and from the blood of these infected horses he extracted 2 Gm.—about one-half teaspoonful—of a whitish powder which he named Krebiozen. The full details of the method of extraction have never been revealed. Later, Dr. Durovic brought this powder to the United States. Here, without prior chemical analysis of the powder, he dissolved it in no. 9 mineral oil in the ratio of one part of Krebiozen to 100,000 parts of mineral oil. Thus he made the original (and only) supply of Krebiozen amounting to 200,000 doses, 1 cc. each.

III. The Men Behind Krebiozen

*Dr. Stevan Durovic**.—Born in Ulcinj, Yugoslavia, in 1905, Dr. Durovic received the degree of Doctor of Medicine from the University of Belgrade in 1930. He did postgraduate work at the University of Vienna and at the Pasteur Institute in Paris. During World War II, as a captain in the Medical Corps of the Royal Yugoslav Army, he was taken prisoner by the Italian army and was held for 18 months. In 1942, on the basis of his being a physician in ill health, he was released and he traveled to Spain and Argentina on a Yugoslav passport with a Vatican visa. In 1944 in Buenos Aires, he established Duga, S. A., which was financed by his brother Marko Durovic, a former munitions manufacturer. At the Duga laboratories he prepared a "whitish powder" which he named Kositerin and which he thought was useful for treating high blood pressure. Dr. Durovic visited the United States in March, 1949, for the purpose of working with doctors at Northwestern University in testing Kositerin. Kositerin was found to be without value for the treatment of high blood pressure.

In August, 1949, Dr. Durovic met Dr. Andrew C. Ivy, a distinguished medical researcher and vice-president of the University of Illinois. At this time Dr. Durovic told Dr. Ivy about another substance, Krebiozen, which he believed was effective against cancer, and he solicited Dr. Ivy's help in testing the drug.

Dr. Durovic is not licensed to practice medicine in this country. He has stated that he is interested only in research, but he has not published in any scientific or medical journal in this country during his nearly 10 years of residence here. In July, 1952, he was granted permanent residence in the United States through Senate Bill 1159, sponsored by Senator Paul Douglas of Illinois. In September, 1958, he became a naturalized citizen of the United States.

Dr. Andrew C. Ivy.—Born in Farmington, Mo., in 1893, Dr. Ivy received his Ph.D. from the University of Chicago and his M.D. from Rush Medical College. He has been the author or co-author of many published scientific articles. Numerous honorary degrees have been awarded to him, and he has held important posts in several universities, in the government, and in private organizations. He was at one time scientific director of the Naval Medical Research Institute, executive director of the National Advisory Cancer Council, and consultant (on war crimes) to the Secretary of War. When he met Dr. Durovic in 1949, he was vice-president-in-charge of the Chicago Professional Colleges of the University of Illinois and distinguished professor of physiology and head of the department of clinical science at the university.

Although he had not previously published any papers on Krebiozen in medical journals, at a meeting in the Drake Hotel in Chicago on March 26, 1951, attended by physicians and laymen including members of the press, Dr. Ivy submitted a privately printed, 106-page brochure which favored Krebiozen and of which he was co-author. The meeting was widely publicized in newspapers and there was a public furor over Krebiozen. Because of the methods Dr. Ivy had used to promote Krebiozen, his membership in the Chicago Medical Society was suspended for three months. Although he was later invited to reinstate his membership, he declined to do so and was dropped from the roster of the society for nonpayment of dues. This action automatically terminated his membership in the Illinois Medical Society and the American Medical Association.

Dr. Ivy has stated that the process of manufacturing Krebiozen has not been revealed to him and that he has neither seen nor analyzed the original substance in the undissolved state. He has also stated that in Chicago he has extracted a substance from 40 horses, recreating by deduction the process that Dr. Durovic used to extract Krebiozen in Argentina. Dr. Ivy is reported to have obtained 10 times the amount of powder that Dr. Durovic claimed to get from the same number of animals. However, since the composition of Dr. Durovic's powder has never been revealed, there is no way of knowing whether the substance extracted by Dr. Ivy in the United States in 1957 is the same as that obtained by Dr. Durovic in Argentina eight years before.

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*Details of Stevan Durovic's career before he came to the United States are based on a pamphlet published in June, 1953, by the Krebiozen Research Foundation, and on a letter, now in the files of the National Cancer Institute, from the foundation's secretary.

Several other physicians in association with Dr. Ivy have privately published monographs on Krebiozen. These men are Dr. J. F. Pick, a plastic surgeon; Dr. W. F. Phillips, a general practitioner; and Dr. L. Krasno, a researcher in antibiotic dusts.

*Marko Durovic**.—Born in Ulcinj, Yugoslavia, in 1900, Marko Durovic, brother of Stevan Durovic, received his legal training at the University of Paris and the University of Belgrade, completing his training in 1923. In 1926 he was appointed judge in the Yugoslav District Court in Belgrade. He practiced law from 1927 to 1941 and was co-owner of Vistad, a munitions plant. In 1942 he was seized by Italian troops and was sent to Rome. Through the intercession of the Vatican he was released and allowed to travel to neutral Argentina with his brother. There he bought a steel plant and the Instituto Biologica Duga and underwrote his brother's experiments which produced "Kositerin." He came to the United States in 1950 on a visitor's visa. In July, 1952, he was granted permanent residence in the United States through Senate Bill 1159, sponsored by Senator Paul Douglas of Illinois. In September, 1958, he became a naturalized U. S. citizen.

IV. Organizations Connected with Krebiozen

A number of organizations have been created by the supporters of Krebiozen to publicize, promote, and distribute the drug and/or to obtain public support for the testing of Krebiozen according to the terms laid down by its proponents. These organizations are:

1. Duga Laboratories, Inc., Chicago, and Buenos Aires, Argentina. This drug firm was established by Marko Durovic to underwrite Dr. Stevan Durovic's experiments which produced Krebiozen. Duga Laboratories, Inc., distributes Krebiozen to physicians through the Krebiozen Research Foundation (see below), which it supports. Duga Laboratories, Inc., accepts from the foundation moneys which the foundation receives as contributions from patients who have been given Krebiozen. According to Herbert Bailey's "A Matter of Life or Death," Dr. Durovic has stated that the Duga Laboratories, Inc., is in debt to creditors who expect to receive a return on their investments if Krebiozen is proved to be an effective cancer remedy.

2. The Krebiozen Research Foundation, Chicago. This foundation is registered in the state of Illinois as a nonprofit corporation. It furnishes Krebiozen to selected physicians for use in treating patients. The necessary steps under the Public Health Service Act have never been taken to make it possible for Krebiozen to be sold for use in interstate commerce (see section VII). However, the recipient is requested to make contributions to the Duga Laboratories, which supports the foundation. The request for contributions is at the rate of $9.50 per ampul. The Foundation Library Center reports that as of February, 1959, the Krebiozen Research Foundation had not published a list of officers, a report of activities, or a financial statement.

3. Committee for Independent Cancer Research, Inc. Originally formed ostensibly to investigate various cancer remedies, this organization has put forth major efforts to promote Krebiozen and a book "Krebiozen, Key to Cancer?" written by Herbert Bailey, president of the committee. Because of a disagreement over a matter of policy, this committee has since split into two divergent groups: (*a*) The Freedom for Cancer Research Committee. Mr. David M. Kasson, who claimed he had been treated for cancer with Krebiozen, presided over this committee. Upon his death from cancer in June, 1958, the committee was dissolved. (*b*) The Independent Cancer Research Foundation, Inc. Miss Gloria Swanson, former chairman of the Committee for Independent Cancer Research, serves as a member of the board of directors. This group is devoted to gathering and disseminating "all possible information on trends in cancer research and treatments."

4. Committee for a Fair Test of Krebiozen, Inc. This group has circulated petitions urging the American Cancer Society to support the method of testing of Krebiozen which its proponents are demanding.

5. The Lakeland Foundation of Chicago. This organization has also been involved in the Krebiozen controversy. According to the Foundation Library Center it is a private corporation and is incorporated under a broad charter that includes conservation of natural resources, care of the aged, research in economic science, and medical research in the field of malignancy. The Lakeland Foundation does not currently publish an annual report.

The Lakeland Foundation has come to Dr. Ivy's assistance on two occasions. When he was on a leave of absence from Jan. 1 through June 30, 1953, from the University of Illinois and without salary, the foundation loaned him $5,000 for living expenses. In 1956-1957, the Lakeland Foundation advanced the sum of $10,000 to Dr. Ivy for the purpose of recreating Krebiozen.

V. Has Krebiozen Ever Been Tested?

1. (*a*) The powder form of Krebiozen was never chemically analyzed before being dissolved in mineral oil. An analysis of Krebiozen dissolved in no. 9 mineral oil has been done by the Clark Microanalytical Laboratory, Urbana, Ill., and was reported in *Chemical Week*, June 16, 1956. According to the Clark analysis, "It contained no nitrogen and . . . might contain some sulphur in addition to carbon, hydrogen and oxygen. Infra-red and ultraviolet

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*Details of Marko Durovic's career before he came to the United States are based on a pamphlet published in June, 1953, by the Krebiozen Research Foundation, and on a letter, now in the files of the National Cancer Institute, from the foundation's secretary.

spectroscopy revealed absorption bands indicating that it could be either a polysaccharide or a steroid. A further study of the product is required before a more definitive statement about its chemical structure can be made."

(*b*) Two distinguished chemists, Drs. Paul Kirk of the University of California and Arthur Furst of Stanford University, testified at the 1958 hearings of the California General Assembly Committee on Public Health that they had independently attempted to extract and to analyze Krebiozen. After the most exhaustive tests Dr. Kirk independently concluded that "the extraction failed to reveal the presence of anything dissolved in the ampules and would lead to the supposition that all that is contained in Krebiozen is mineral oil, Nujol, to be specific, because the analysis indicated the identity with Nujol." Dr. Furst concurred. "I say it is pure Nujol," he stated.

Dr. Ivy has challenged this testimony.

2. (*a*) A few animal studies have been done with Krebiozen by its proponents. From these studies it is claimed that the substance is nontoxic in rats, cats, and dogs.

(*b*) Twelve dogs were said to have been treated with Krebiozen by Dr. Hannibal DeGrana at the School of Veterinary Medicine of the University of Buenos Aires. All the animals were described as having natural cancer; seven animals were said to be almost blind because of cataracts. It was said that all of the tumors were affected to some degree and that in six dogs the cataracts cleared and the dogs regained sight.

(*c*) John B. Loefer, Ph.D., of the Southwest Foundation for Research and Education, San Antonio, Texas, reported on the effects of Krebiozen therapy on transplanted mouse leukemia and lymphosarcoma in The Journal of the American Medical Association on May 17, 1952. "Krebiozen . . . did not affect the course of development of either the leukemia or the lymphosarcoma," he wrote.

3. (*a*) In 1952, the Committee on Research of the Council of Pharmacy and Chemistry of the American Medical Association published "A Status Report on Krebiozen" in The Journal of the American Medical Association. This report, made by a group of four distinguished educators from several medical schools in Chicago (excluding the University of Illinois), contained an analysis of 100 case histories of patients treated with Krebiozen. The case records had been received from seven sources and were examined at the request of Dr. Ivy and his associates at the Krebiozen Research Foundation.

"Ordinarily, the Committee on Research . . . would not attempt to evaluate the clinical benefits, if any, of a substance whose character and method of manufacture were not known and standardization of which was so loosely defined," the A. M. A. report stated. "However . . . tremendous worldwide public interest created a moral obligation . . . which transcended the issue of medical ethics ordinarily applicable to secret remedies."

The conclusions of this report were:

"Ninety-eight (of 100 cases studied) were reported as failing to show evidence of improvement.

"Two patients showed some evidence of temporary improvement coincident with Krebiozen therapy. In one patient this was apparently fortuitous; in the other major lesions showed continued rapid progression."

(*b*) Seven investigators reported on 63 cancer cases treated with Krebiozen to the Committee on Cancer Diagnosis and Therapy of the National Research Council. The committee then reviewed these and other cases in 1951 and found "no evidence of any curative effect and no proof of palliative effect attributable to the 'drug' itself." This opinion was based on an analysis of the 100 cases already reported in The Journal, some of which were included among the 63 cases studied by the Committee and the 22 cases reported by Dr. Ivy and others in the booklet distributed at the meeting in the Drake Hotel on March 26, 1951, when Krebiozen was first announced.

(*c*) In 1952, a committee of six distinguished physicians from several medical schools, headed by Dr. Warren H. Cole, head of the department of surgery of the University of Illinois, was appointed by Dr. George Stoddard, president of the university, for the purpose of reviewing Dr. Ivy's 500 cases of cancer treated with Kreboizen. The committee's report, presented to the trustees of the university, contained the following significant conclusions: "Ignorance of the material interferes with a sound evaluation of its therapeutic effectiveness . . . no acceptable evidence that any malignant tumor had been cured by Krebiozen . . . no evidence of prolongation of life . . . no histological evidence that Krebiozen produced degenerative or regressive changes in tumor cells . . . no radiographic evidence that Krebiozen could reduce metastatic tumor lesions in bones or lungs . . . statement in Dr. Ivy's report that a large majority of patients reported a decrease in pain was not confirmed."

In a discussion of future tests, the Cole committee advised that a supply of Krebiozen should be made available for testing and that investigators should attempt to reproduce the material and determine its chemical content.

(*e*) A committee of supervision, under the chairmanship of Dr. Robert E. Johnson, head of the department of physiology, Urbana, Ill., was appointed by Dr. Stoddard to carry out the recommendations of the Cole committee. The committee of supervision reported in part that "a supply of the original material was needed so that it could be tested directly. A supply of the vehicle was needed for adequate scientific control. Complete information on the mode or modes of preparation was needed

. . . the originators of the preparation are unwilling to furnish materials and will not provide full technical information . . . (therefore) the committee is unable to proceed further."

(*f*) In 1952, after a 21-month investigation, Dr. Stanley P. Reimann, director of the Institute for Cancer Research, Philadelphia, announced: "We now know we have cured no patients [with Krebiozen] and we don't believe the length of life has been prolonged on any we have treated."

4. The proponents of Krebiozen have been involved in legislative investigations in two states and have received support from at least two U. S. Senators and one U. S. Representative.

(*a*) The Illinois legislature: In 1953, a joint committee of 14 Illinois legislators was appointed from the two state legislative bodies to investigate the Krebiozen controversy. In 1954, after extensive hearings for which records were subpoenaed, this committee concluded that Dr. Ivy and the Durovic brothers "were men of good character" and that neither Dr. Stoddard nor the American Medical Association had conspired against Dr. Ivy. The committee urged further research on Krebiozen but made no recommendations as to how this research was to be conducted.

(*b*) The California Senate: In 1958, the California Senate Committee on Public Health held hearings on "Fraudulent, Dangerous, Unscientific and Deceptive Practices in the Field and Treatment of Disease" at which Dr. Ivy testified. The burden of Dr. Ivy's testimony was directed to the advocacy of a "double-blind" test of Krebiozen which its proponents have been endeavoring to get.

(*c*) The late Senator Charles W. Tobey: Senator Tobey is reported to have sponsored an investigation of Krebiozen by a staff investigator.

(*d*) The Honorable Roland V. Libonati, U. S. Representative from the State of Illinois: On several occasions, Congressman Libonati has had remarks on Krebiozen inserted in the Congressional Record. His remarks have generally echoed Dr. Ivy's.

(*e*) Senator Paul Douglas of Illinois: Senator Douglas sponsored a bill in the U. S. Senate which gave the Durovics permanent residence in the United States. On the floor of the United States Senate, in August, 1958, Senator Douglas proposed a "Fair Test of Krebiozen" to be done by the National Institutes of Health, a U. S. Government institution. Later, Drs. Ivy and Durovic met with Dr. Heller, director of the National Cancer Institute of the National Institutes of Health, and with a representative of Senator Douglas. At this meeting, Dr. Heller stated that "the first step should be an examination of the case records in possession of the Krebiozen Foundation."

At a meeting on Sept. 24, 1958, attended by Drs. Ivy and Durovic, Senator Douglas's representative, and Dr. Heller, it was generally agreed that the evaluation of Krebiozen should be explored further and that the group was seeking to develop an agreed procedure that would be acceptable to the scientific community.

On Dec. 5 at another meeting attended by the same group, this time including Senator Douglas, the National Cancer Institute suggested an examination of Dr. Ivy's data by a committee of mutually acceptable scientists to decide whether clinical trials should be undertaken and how they should be undertaken. Senator Douglas expressed the opinion that this suggestion was a proper one. Dr. Ivy was invited to define his role as consultant to the evaluating committee, to which he had agreed.

He answered in a letter to the Institute dated Feb. 1, 1959, insisting that he personally should be a member of "an arbitration type of committee" and "a party to the administration of the therapy and the interpretation of the results under conditions where bias cannot operate." This is a procedure which, as pointed out in two conferences attended by Dr. Ivy, could admit bias and would not be acceptable to the scientific community.

The Institute responded to Dr. Ivy's letter on Feb. 6 by asking him to clarify his apparent rejection of the previous plan made between him and the National Cancer Institute, because "it is the desire of the Institute to get on with the evaluation of Krebiozen as soon as a scientifically acceptable procedure can be effectuated."

VI. Can Krebiozen Be Tested?

The proponents of Krebiozen have frequently stated that they would welcome an evaluation of their preparation, and during the last two years they have conducted an active campaign to promote a specific type of evaluation which they have outlined as a "double-blind" test.

In the past, an evaluation of Krebiozen by independent researchers has been obstructed because of lack of information about the substance and its preparation and the unavailability of the substance. Thus, the Committee on Supervision, which was appointed at the University of Illinois in 1952, was unable to proceed with an evaluation of Krebiozen.

Also, independent evaluation of Krebiozen has been impeded because of inadequate information about the drug, the unwillingness of its proponents to surrender to independent researchers the case histories on which they base their claims, and the insistence of the proponents that Krebiozen be tested only on the terms which they themselves have set forth—terms which have been unacceptable to reputable scientists unassociated with Krebiozen.

Recently, the supporters of Krebiozen have concentrated their propaganda efforts on trying to get a reputable organization to sponsor a "double-blind" study of their substance.

The proposal for such a study was first made to the American Cancer Society in 1958 by James L. Griffin, Director of the Krebiozen Research Foundation.

Briefly, the study proposed by Mr. Griffin called for the appointment of a committee of laymen and a committee of physicians, one-half of the members of each committee to be selected by the Krebiozen proponents and one-half to be chosen by the American Cancer Society. Each committee would then select a single additional member. Ampuls of plain mineral oil and ampuls of Krebiozen identified only by code numbers would be administered by Dr. Ivy to known cancer patients. The extra member of the lay committee would be the only person to know the identity of the contents of the ampuls, and he would be instructed to keep the code list in a safety deposit box.

At the end of the period of treatment Dr. Ivy would evaluate the results and undertake to identify the patients who had received Krebiozen and those who had not. Committee members would be permitted to observe the patients and to take notes during the treatment period.

The Krebiozen proponents claim to have 1,200 case records of patients already treated with Krebiozen. In testing an unproved substance, the first step would be to evaluate the results already achieved, and in this case it would mean an analysis of the alleged case records. In its proposal to the American Cancer Society, the Krebiozen Research Foundation, however, refused to permit an examination of these case records, unless the Society agreed beforehand to sponsor their suggested study.

Their proposal for this particular study was carefully considered by the American Cancer Society's Advisory Committees on Research and on the Therapy of Cancer and by the Society's Research Advisory Council. These three groups of scientists concluded that this proposal "does not provide a scientifically valid plan for conducting an objective and meaningful evaluation." Their opinion was adopted by the Board of Directors of the American Cancer Society on Oct. 24, 1958.

The first reason for rejecting the proposal was that the committees to be set up as outlined by the Krebiozen proponents would not be truly independent research groups, because one-half of the membership of each committee would consist of individuals selected by the proponents.

The second reason was that the plan stipulated that only Dr. Ivy would administer the Krebiozen. The American Cancer Society felt that this would not permit "an opportunity to determine whether physicians generally can obtain the same results."

The third reason for rejecting the proposal was that the plan "provides no clear-cut standards for either measuring the result desired or defining or measuring the results obtained."

The Society further stated that it would be willing to support "the testing of any substance proposed for the prevention, treatment, or cure of cancer, provided the substance is available for testing under the well-established scientific methods known and accepted for all products proposed for human use, and further, provided that satisfactory preliminary evidence exists that the substance has shown promise of being useful in the treatment of cancer."

The American Cancer Society itself cannot test any drug. It does not operate research laboratories, nor does it control hospitals or other facilities for the treatment of cancer patients. The Society has clearly made it a matter of record that it favors the full knowledge and testing of Krebiozen.

VII. Is Krebiozen Patented? Can It Be Sold?

The owners of Krebiozen have stated on numerous occasions that they have a large investment in this substance and intend to market it for profit. For this reason they are concealing the details of the manufacturing process, thereby setting up a barrier to the testing of the substance by independent researchers.

If the owners of Krebiozen wish to protect the substance, they may apply for a patent on it. They may also apply for a patent on the process by which it is made. Hundreds of drugs are manufactured in this country under such patents.

Such applications are temporary protection for the proponents while the patents are being searched.

Some years ago the owners of Krebiozen applied for a patent but when the U. S. Patent Office returned the application with request for further information, the owners of Krebiozen failed to supply this information and did not resubmit their application. Hence, there is no patent or new application for a patent on Krebiozen, either the substance or the process, in the files of the U. S. Patent Office as of January, 1959.

By its description Krebiozen is subject to the biological control provisions of the Public Health Service Act and thus it may not be legally shipped for sale, barter, or exchange in interstate commerce or exported from or imported into the United States, unless it is produced under government license. No application for such license has ever been completed for Krebiozen. If an application were made, supported by adequate evidence of safety, purity, and potency of the product, it would be the responsibility of the Division of Biologic Standards of the National Institutes of Health to recommend whether or not a license should be issued. Without this license Krebiozen may be distributed only to qualified experts, solely for purposes of clinical investigation, but it cannot be sold. Some physicians, as indicated in section IV, have obtained Krebiozen in this way since 1952.

VIII. Publicity and Promotion of Krebiozen

The history of Krebiozen has presented elements both of wide publicity and of deep secrecy. Some of the proponents, although they are physicians and well acquainted with the accepted procedures for introducing a new substance, have ignored and flouted these procedures in the case of Krebiozen. From the very first they have sought to arouse the public interest in Krebiozen before adequately demonstrating to the medical profession the utility or efficacy of the substance.

For this unorthodox approach, Dr. Ivy was disciplined by the medical society of which he was a member. He consequently was relieved of his position as vice-president of the University of Illinois. Such censure, however, has not deterred him from continuing to publicize Krebiozen. He has since appeared on television and radio programs devoted to the promotion of the drug, has held interviews with the press, and has made other public appearances in behalf of Krebiozen.

An example of Dr. Ivy's methods of attracting publicity is provided by the circumstances of his recent letter to Dr. Harold S. Diehl, senior vice-president for research and medical affairs of the American Cancer Society, proposing a test of Krebiozen. Dr. Ivy was not content merely to communicate privately with Dr. Diehl. At the time he sent this letter, he also released copies of it to the press in an obvious effort to create publicity.

The press releases that have been issued by the proponents of Krebiozen, or in their behalf, are not always consistent with the facts. For instance, G. P. Putnam's Sons, publishers of the new book "A Matter of Life or Death, the Incredible Story of Krebiozen" by Herbert Bailey, issued a press release stating that "'the evaluation of Krebiozen—the controversial anticancer agent—by the National Cancer Institute is under way and will proceed with all possible speed,' Dr. John R. Heller, the Institute's Director told Herbert Bailey (sic)." This release, dated Nov. 11, 1958, also declared that the National Cancer Institute had agreed to conduct a "double-blind" test of Krebiozen. Herbert Bailey, who apparently prepared the Putnam release, had sent a copy of it, prior to its publication, to Dr. Heller for his suggestions. Dr. Heller answered immediately, on Nov. 6, 1958, correcting two inaccuracies in the copy: (1) the evaluation of Krebiozen is not under way, and (2) the method of testing has not yet been agreed upon and cannot be determined until examination of data has been completed. "Actually," wrote Dr. Heller, "we are now approaching the preliminary stage of examining the data submitted by Dr. Ivy to determine whether it warrants further investigation of the treatment."

Although Dr. Heller's comments were sent to Mr. Bailey five days before the press release was published, Mr. Bailey replied that they were received too late for the necessary revisions to be made.

It has also been pointed out by Dr. Heller that on Sept. 24, 1958, when he and other members of the National Cancer Institute met with Drs. Ivy and Durovic to discuss the testing of Krebiozen, Drs. Ivy and Durovic subscribed to a press release issued by the National Cancer Institute which stated that the method of testing Krebiozen should be acceptable to the scientific community. At that meeting, there was no agreement to undertake the "double-blind" study proposed by Dr. Ivy and which had already been widely rejected by scientific investigators.

IX. National Cancer Institute Requirements

The conditions under which the National Cancer Institute would consider an investigation of Krebiozen are based on principles long accepted by the scientific community at large. They apply to the testing of any drug, the value of which has not been adequately proved. These accepted conditions were first outlined by the National Advisory Cancer Council as guide lines for the National Cancer Institute in evaluating compounds and are subscribed to by the American Cancer Society. They are the following:

1. The chemical formula, if known, must be disclosed to the National Cancer Institute, or if not known, the method of preparation must be supplied.
2. Adequate amounts of the chemical having known purity must be available.
3. The evidence upon which any claim of efficacy is based must be presented along with a full explanation of the method of treatment.
4. The National Cancer Institute reserves the right to determine if, how, where, when, and by whom the investigation is to be carried out.
5. The scientists making the investigation will have the right to publish the results.

The National Cancer Institute is willing to undertake an evaluation of claimant's data on an unorthodox treatment claimed to effect cancer cures in humans, provided that the following conditions are accepted:

1. The method of treatment must be fully explained. There must be full disclosure to the National Cancer Institute of the composition or nature of the treatment.
2. Complete records of clinical and laboratory findings must be submitted of the total number of patients with cancer treated with the remedy or method in question. These records must demonstrate the following: (*a*) Diagnosis of cancer in each case, confirmed by verifiable microscopic examination. (*b*) Detailed and documented objective evidence that malignant neoplastic disease has disappeared or that its progress has been arrested for a significant period of time in a significant number of patients. It must be shown that no definitive treatment other than the one in question was used during this period of observation; in addition, a detailed record of all treatment received by the patients prior and subsequent to the test period must be supplied. (*c*) Details as to preparation, dosage, frequency, and route of administration of the agent in question. (*d*) Complete details as to physical and supportive laboratory findings and histological studies in the patients prior to, during,

and subsequent to the course of and cessation of the treatment in question. (c) Objective evidence of regressions of primary tumor and metastases as shown by recorded measurements of observable tumors, photographs, and x-rays, with dates of observation.

3. The National Cancer Institute reserves the right to determine whether or not the evidence submitted warrants further investigation of the proposed treatment and its results and reserves the right to determine where, when, by whom, and under what conditions such investigation will be made. The National Cancer Institute reserves the right to make public its findings.

X. The American Cancer Society and Unproved Drugs

Under the American Cancer Society's research program, hundreds of organic and inorganic compounds have been screened and a few substances have been found which are palliative in certain types of human cancer. The results of research on all of them were first published in medical journals. All of these substances can be manufactured by a drug concern and all are readily available to doctors and to hospitals for experimental purposes.

The American Cancer Society is dedicated to the task of finding the cause and the cure of human cancer at the earliest possible moment. To this end, it supports scientific investigation of every promising kind. At the same time, however, it has the responsibility of seeing to it that the public is not misled by enthusiastic claims of individuals who would exploit unproven methods or drugs for the treatment of cancer. Ill-advised reliance on such unproven methods or substances militates against possible cure of the disease by the acceptable methods known at the present.

Any drug which is claimed to cure cancer must fulfill certain objective criteria. Krebiozen has not met these standards. No acceptable evidence that treatment with Krebiozen causes any objective benefit in human cancer has yet been offered by independent researchers.

XI. Conclusions

Advocates of Krebiozen have demanded through all publicity channels what they describe as a "fair test" of the drug. The National Cancer Institute of the United States Public Health Service is willing to conduct a test to further evaluate Krebiozen but insists that it be done in a manner acceptable to the scientific community.

The Krebiozen Research Foundation, Dr. Ivy, Dr. Durovic, and their associates have long claimed they have a tool useful against cancer: it is, then, their clear duty to thousands of cancer patients to cooperate with the National Cancer Institute or any group of competent, objective scientists in an objective test of the drug. Delays now are clearly the responsibility of the Krebiozen Research Foundation.

When Krebiozen was first announced, it was tested in hospitals, clinics, and laboratories, according to scientifically accepted procedures. The results of the tests carried out by scientists and clinicians were reviewed in reports mentioned in section IV. This avenue of testing still remains open to advocates of Krebiozen.

However, the agitation continues. This has an unsettling effect on cancer patients, their families and friends, who question whether the extraordinary claims about Krebiozen are true. The answer can only be settled by a thoroughly objective study such as the one the National Cancer Institute has indicated it is willing to make.

The American Cancer Society hopes that the Krebiozen Research Foundation will recognize the integrity of the National Cancer Institute of the United States Public Health Service and respect its well-established methods and procedures and that the foundation will drop its demands for its own rules and procedures.

THE WORLD'S PLAYGROUND

Known for three generations as the world's playground, Atlantic City has the world's largest compact playground for children, seven miles of beach blocked off by a boardwalk on which no auto traffic is allowed. When physicians gather in Atlantic City, June 7-12, for the convention of the American Medical Association, many will bring their wives and children. The city has merry-go-rounds, Ferris wheels, auto whips, boat rides, caterpillar thrills, airplane rides, tilt-a-whirls, and other breath-taking amusements. Dotting the Boardwalk are Pennylands and Funlands where youngsters can find delights all day for nickels and dimes. They can play miniature baseball and basketball, ride "jet" airplanes and submarines, and hunt miniature moving bears and lions. They can try to ring a prize, test their bowling prowess, or push around golf balls on miniature courses decorated with Disney or Mother Goose characters.

Steel Pier is also a happy place for children. Appealing to adults as well are its famed diving horses, which leap from a 40-ft. platform into a tank with girl riders astride their bare backs, and its water circus with crazy clowns. Steel Pier also has a sea-zoo, a children's theater, a Ripley's Believe-It-or-Not exhibit, and a picnic deck.

In addition to the special programs provided by Atlantic City's hotels and motels, the resort also has in operation during the summer 21 children's playgrounds, as well as shuffleboard courts, bowling alleys, and roller skating rinks, which older children can enjoy. The Boardwalk also has dozens of stores specializing in novelties and toys. In June, when the physicians will be here for the big A. M. A. powwow, manufacturers and distributors will be stocking these stores with new toys.

THE LEISURE CORNER

FLYING PHYSICIANS

Man's desire to achieve flight has been evident from early times. Myths and legends of many peoples relate adventures in flying, one of the most familiar being the Greek myth of Daedalus and Icarus. In the 13th century Roger Bacon proposed the construction of a flying machine with wings that could be operated by the person being carried. The detailed observations, explanations, and drawings found in the notebooks of Leonardo da Vinci mark the beginning of scientific studies of flight. Flight was first successfully accomplished in 1783 in a lighter-than-air device today known as a balloon.

At the beginning of the present century aviation was still in its infancy. Only a handful of men were interested even in gliding. When the Wright brothers made their first flight in a powered, heavier-than-air craft in 1903, they stayed in the air only a few seconds. Today the airplane has created a vast and growing industry, revolutionizing travel and warfare and bringing about tremendous changes in commerce, science, international politics, and the world's standard of living.

Insofar as flying pertains to the practice of medicine, stories about mercy flights to save lives have become commonplace in newspaper accounts. Physicians and nurses have been flown into areas cut off by floods, fires, and other disasters. Sick and injured people have been flown from their homes to hospitals hundreds of miles away in a short time. Moreover, airplanes and helicopters have been equipped as flying ambulances and are used to hunt for and rescue persons lost in forests, at sea, or on mountains. Special drugs, medicines, and isotopes are transported quickly in emergency situations, whereas without the airplane the matter would be time-consuming.

As a hobby for doctors, an excellent way to get off crowded highways and enjoy the wondrous beauties of the wide blue yonder is to own and fly a private airplane. There is much difference between piloting a small private airplane and traveling on a large commercial aircraft. An individual flying on his own must learn the art, get accustomed to the air, and depend on his own skill and judgment. The attributes of skill and judgment should not be alien to a physician, since he is always confronted by situations requiring their application in daily medical practice.

Many persons find they can solo after about eight hours of dual instruction. Experience accumulated during a period of preliminary flight training usually will influence one either to continue with enthusiasm or to drop completely the idea of pursuing further the hobby of flying. One of the most frequent causes for giving up flying a small airplane is the fear of becoming lost, especially during heavy fog. Although the experience of being lost is sometimes terrifying, most flyers regain their confidence quickly.

The student pilot immediately becomes aware that it is not the engine alone but the entire shape and construction of the airplane that cause it to fly. To illustrate, gliders fly without the aid of engines. The beginner must therefore learn something about the nature of air—that it will hold him up just as water holds a swimmer up when he acquires confidence and learns to handle himself properly. Too many people think of a small airplane in terms of an automobile or a motor boat, to be steered around all the curves. The truth is that an airplane is more like a bicycle, which has to be balanced around curves.

You will find that when you pilot your own airplane you will see much more than when you were a passenger on a huge commercial airliner. The need for seeing is important; the pilot needs to see where he is going. In addition, say the owners of private airplanes, the ability to see the surroundings is the very heart of the pleasure to be derived from piloting a private airplane.

Ordinarily, it is not advisable to buy an airplane at the first flush of one's original enthusiasm for flying. The situation is not comparable to buying an automobile in order to learn how to drive it. It is best to learn the art of flying at a reliable flying school. Then, when this is accomplished satisfactorily, the next step is to rent an airplane; under these circumstances, the owner of the airplane will be justifiably concerned for the safety of the pilot. Eventually the pilot will be able to evaluate the characteristics of small airplanes and will be ready to consider purchasing his own.

After a sufficient period of practice in the air the new pilot realizes that he is obtaining an entirely fresh view of the countryside, together with a thrilling, exuberant feeling of well-being and personal satisfaction. Many private pilots take trips to North Dakota. When asked why, they answer: "The landings are unlimited, as far as the eye can see; the fields are big and flat as a table, much larger than airports." When planning a vacation in a private airplane, there arises always the possibility of viewing new vistas and aspects of the United States hitherto unseen and unvisited. Everything the flying physician will want to see is within easy flying distance, no matter what the point of origin. California can be reached from Chicago in easy, relaxed hops; the trip from Chicago to New Orleans requires but one day of solo flight; the trip from Seattle to San Francisco is delightful and takes merely a few hours. Flying in a private airplane can become the most liberating of all hobbies.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Cardiac Catheterization: Risks, Inconveniences, Indications and Contraindications: Study Based on 500 Observations. F. Rovelli. Minerva med. 49:4102-4111 (Nov. 3) 1958 (In Italian) [Turin, Italy].

The author reports on 500 cardiac catheterizations performed for diagnostic purposes on 469 patients, between 4 months and 52 years of age, with congenital or acquired cardiopathy. Of 231 patients with acquired cardiopathy, stenosis of the mitral valve was present in 98, defect of the mitral valve associated with other disturbances in 104, constrictive pericarditis in 16, and other disorders in 13. Of 238 patients with congenital cardiopathy, cyanosis was present in 81. Cardiac catheterization was carried out in 68 patients while they were under general anesthesia. In the course of cardiac catheterization, venous spasm developed in 3 patients and arrhythmia in 50. Episodes of nodal and atrial extrasystoles were common but well tolerated. Atrial fibrillation developed in 1 patient and paroxysmal tachycardia in 2. Acute pulmonary edema developed in 4 patients—in 2 during and in 2 after the catheterization. Complications after use of the catheter included chills (which developed in 19 patients), mild febrile episodes (in 75), and benign phlebitis of veins of the arms (in 8). The deaths of 3 patients, which can be attributed to use of the catheter, were related to pulmonary edema in 2 and to cardiac arrest because of anoxemia, which developed during the anesthetic state, in 1.

To minimize complications of cardiac catheterization, the author suggests the use of flexible catheters, careful sterilization of the catheter, precise premedication, application of gas narcosis and possible blood transfusions for children, and insertion of the catheter into the left basilar vein or into the saphenous vein if the basilar vein is too narrow. He also suggests infusion of apyrogenic solutions, the strict observance of asepsis, use of electrocardiograms, roentgenologic observations, and oximetry during the procedure, if possible, limiting the duration of the catheterization to as short a period as possible, and performance of the catheterization by an experienced team. Cardiac catheterization is a valuable therapeutic tool, but its application must be individualized, taking into aaccount its limitations and hazards.

Experiments on the Antituberculous Activity of Alpha-Ethyl-Thioisonicotinamide. N. Rist, F. Grumbach and D. Libermann. Am. Rev. Tuberc. 79:1-5 (Jan.) 1959 [New York].

The antituberculous activity of alpha-ethyl-thioisonicotinamide has been tested in vitro and in experimental animals. Although this compound is a derivative of isonicotinic acid, it is not a derivative of isoniazid. It has proved to be highly active both in vitro and in vivo against strains of tubercle bacilli that are resistant to isoniazid. It is 4 times more active in vivo than thioisonicotinamide, but its toxicity is not greater than that of the latter compound. Qualitatively, the effect induced by alpha-ethyl-thioisonicotinamide is similar to that of isoniazid; quantitatively, it is twice as effective as streptomycin and one-tenth as active as isoniazid in experimentally infected guinea pigs. Its toxicity in mice is only one-fifth that of isoniazid. When alpha-ethyl-thioisonicotinamide is administered by the oral route to man, it has been found in the serum in a biologically active form. The results of these studies accordingly justify the clinical trial of this compound.

Observation on the Antituberculous Effectiveness of Alpha-Ethyl-Thioisonicotinamide in Tuberculosis in Humans. G. Brouet, J. March, N. Rist and others. Am. Rev. Tuberc. 79:6-18 (Jan.) 1959 [New York].

A clinical investigation was carried out with the administration of alpha-ethyl-thioisonicotinamide in 102 patients with pulmonary tuberculosis; 73 were men and 29 were women. Fifty-seven of the patients had recent tuberculosis, and 45 had chronic tuberculosis. A thorough physical examination, roentgenologic study, and culture of sputum and of gastric washings for Mycobacterium tuberculosis had been frequently carried out in each patient. All strains of tubercle bacilli isolated were tested in vitro for susceptibility to alpha-ethyl-thioisonicotinamide, to isoniazid, and to other common antimicrobial drugs. Alpha-ethyl-thioisonicotinamide was administered orally, the usual regimen being 1 Gm. daily, or 4 tablets, given either as 2 tablets

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The place of publication of the periodicals appears in brackets preceding each abstract.

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twice daily or in the individual dosage of 0.25 Gm. at 6-hour intervals throughout the day. This compound was often not well tolerated and gave rise to side-effects, such as anorexia, nausea, or gastric irritation; the patients either ceased to gain weight or actually lost weight. There was no evidence, though, that it had a toxic effect on the liver, the kidneys, or the hematopoietic system, and it seemed to have a minimal neurotoxic activity, which required special attention only in patients treated concomitantly with isoniazid or cycloserine.

The treatment with alpha-ethyl-thioisonicotinamide had a beneficial effect on the clinical course, on the roentgenologic aspects, and on the bacteriological findings of patients with pulmonary tuberculosis. The bacteriostatic effect of this compound was particularly pronounced in patients with recent tuberculosis, and resolution was obtained within 2 or 3 months after institution of therapy in a large number of patients. The action of this drug, however, was not constant. The condition of some patients did not improve, and the emergence of bacterial resistance to alpha-ethyl-thioisonicotinamide occurred in several patients, but without evidence of decreased sensitivity to other bacteriostatic agents. After the administration of other orthodox antimicrobial drugs rapid improvement occurred in these patients.

Alpha-ethyl-thioisonicotinamide should not be administered alone, but only in conjunction with other antibacterial drugs, such as isoniazid, or isoniazid and streptomycin. It was found in this series that the combined treatment was very effective in patients with advanced pulmonary tuberculosis who had been treated previously, and it was active against strains of tubercle bacilli that were resistant in vivo to isoniazid and streptomycin. The authors believe, on the basis of the present experimental clinical investigation, that a study on the triple-drug regimen, consisting of isoniazid, streptomycin, and alpha-ethyl-thioisonicotinamide, is permissible in order to determine more precisely its effectiveness in patients with progressive pulmonary lesions.

Observations on the Administration of Kanamycin to Patients with Tuberculosis. K. W. Wright, A. D. Renzetti Jr., J. Lunn and P. A. Bunn. Am. Rev. Tuberc. 79:72-77 (Jan.) 1959 [New York].

Kanamycin, a new antimicrobial drug which is effective in low concentrations in vitro against tubercle bacilli, has been administered by the intramuscular route to 11 patients with chronic pulmonary tuberculosis. The ages of the patients ranged from 9 to 57 years. Sputum cultures for acid-fast bacilli were positive in all patients, and all strains of tubercle bacilli were resistant to streptomycin, isoniazid, and PAS. The inhibitory blood concentrations were produced and maintained for 8 hours with a daily dose of 0.5 Gm. of kanamycin. Impaired hearing resulted in 2 patients after the daily administration of 1 Gm. of kanamycin. Granular casts appeared in the urine of all patients within 14 or 28 days of treatment. There was no evidence that the drug had a toxic effect on the liver, on the vestibular apparatus, or on the hematopoietic system. No significant sensitivity reaction to the drug occurred in these patients, other than eosinophilia which was common. The rapid appearance of strains of tubercle bacilli highly resistant to kanamycin suggests that in prolonged treatments this drug should be administered only in conjunction with other antituberculous agents. The disappearance of tubercle bacilli from the sputum of one patient and the favorable changes in the sputum volume, in the body weight, and in the chest roentgenograms in some patients indicate that the drug is sufficiently effective to warrant further clinical trial.

Diagnosis and Therapy of Cushing's Syndrome. A. Labhart, E. R. Froesch and W. Ziegler. Schweiz. med. Wchnschr. 89:44-53 (Jan. 10) 1959 (In German) [Basel, Switzerland].

The authors discuss the histories of 10 patients (9 women and 1 man) with adrenal cortical hyperfunction (Cushing's syndrome) observed in the medical clinic of the University of Zurich before October, 1957. Autopsy reports were available in 2 of the cases, and in 7 patients, who had undergone adrenalectomy, the adrenals could be examined. An adenoma was found in the adrenals of 1 patient, whereas the adrenals in the other 8 patients showed hyperplasia. Although in one of these patients the hyperplasia was not detectable on naked-eye inspection, the histological examination in this and the other patients with hyperplasia revealed changes, such as adenoma-like sections in the cortex, obliteration of the cortical stratification, and cellular strands resembling fasciculated tissue. Studies on the hypophysis in the 2 autopsies revealed in one patient a basophil adenoma and in the other slight basophilism, in addition to metastases of a squamous-cell carcinoma. The excretion of hydrocortisone, ascertained on the basis of the 17-hydroxycorticoids, either was greatly increased or was in the upper limits of normalcy, but in 2 patients, in whom the aldosterone excretion was examined, reduced values were found, and one of these had hypopotassemia. The mineralocorticoids were not involved in the hypersecretion, the shifts in the electrolytes and the alkalosis being caused by the hydrocortisone.

An average of nearly 3 years elapsed between the appearance of the first symptoms and the correct diagnosis; in one patient the syndrome was recognized after 3 months. The most frequent of the clinical symptoms of Cushing's syndrome was a plethoric appearance with the characteristic moon-face; this was observed in all 10 patients. Hypogonadism was observed in 6 of the 10 patients: 5 of 8 women had amenorrhea or oligomenorrhea, and the man had impotence and azoospermia. Obesity, particularly of the trunk, was observed in only 4 patients. Hypertension occurred in 6 patients, but it was not severe. Osteoporosis was present in 7 patients and was severe in 2. Typical red striae existed in 4 patients, and 4 others had areas of superficial bleeding. Diabetes, as evidenced in reduced sugar tolerance, existed in 8 patients. Unusual features observed in this group of patients included: a sibship with polyadenomatosis (hyperparathyroidism, islet adenoma, etc.); the occurrence of adrenal hyperplasia secondary to an invasive pituitary adenoma composed of chromophobe-basophilic-mucoid cells; and the association with bronchial carcinoma, with creatinuria and severe muscular dystrophy, with testicular atrophy, and with irreversible secondary adrenal insufficiency after operation on an active adrenal adenoma.

In addition to the cardinal symptoms, the diagnosis of Cushing's syndrome depends on the 48-hour intravenous corticotropin tolerance test with determination of the urinary steroids. Regarding the treatment, the authors say that no reliance can be placed on the rare occurrence of a spontaneous remission, the less so since untreated Cushing's syndrome is usually fatal within 5 years. Irradiation of the pituitary is sometimes effective, but the recurrence rate is high. Bilateral total adrenalectomy and subsequent substitution therapy are presently the treatment of choice of bilateral adrenal hyperplasia.

The Natural History of Tuberculosis in the Human Body: I. The Demonstrable Primary Pulmonary Infiltrate. J. A. Myers. Am. Rev. Tuberc. 79:19-30 (Jan.) 1959 [New York].

A group of 300 children with primary pulmonary tuberculous infiltrates, ranging in age from 2 months to 20 years, were examined between May, 1921, and November, 1941. The primary infiltrates in these children varied in size from those scarcely large enough to be demonstrable to big dense homogenous areas; they were not limited to any lobe or area, some appearing even in the apexes of the upper lobe. The roentgenograms did not visualize characteristic shadows; therefore, differentiation from other diseases, even from the reinfection type of tuberculosis, was rendered difficult. After a few months the primary infiltrates began slowly to resolve, and within a year the shadow-casting lesions disappeared, except for the roentgenologic evidence of calcific deposits at the sites of the original lesion or in the hilar region or both.

Of the 300 children, 267 were followed up; 10 were not examined; and 26 had died. The cause of death was attributed to tuberculosis in 9, the disease being the acute, rapidly fatal forms in 7 (meningitis, pneumonia, and miliary dissemination); the other two patients died of chronic pulmonary tuberculosis 8 and 19 years, respectively, after the primary pulmonary infiltrate was detected. Among the 231 survivors who were examined, the reinfection type of chronic clinical tuberculosis developed subsequently in 9, but it occurred in the region of the primary infiltrate only in 1. The remaining 222 patients have no evidence of any clinical disease.

While mortality and morbidity to date may seem small, it may still be considerably increased, because the subjects under consideration have not lived the halfway mark of natural span of life. The benign character of the demonstrable primary pulmonary infiltrate is no assurance against the development of a chronic disease, because foci that continue to harbor tubercle bacilli may subsequently release organisms that result in clinical lesions.

SURGERY

The Advantages of Early Spine Fusion in the Treatment of Fracture-Dislocation of the Cervical Spine. H. F. Forsyth, E. Alexander Jr., C. Davis Jr. and R. Underdal. J. Bone & Joint Surg. 41A:17-36 (Jan.) 1959 [Boston].

The authors report on 72 male and 9 female patients, between the ages of 8 months and 75 years, with fracture-dislocation of the cervical spine who were considered for internal fixation and spine fusion early in their course of treatment. Fifty-one of the 81 patients sustained their injuries in an automobile accident; the injuries of 12 were produced by falling, those of 6 by diving, those of 3 by gunshot, and those of the remaining 9 by miscellaneous causes. Of these 81 patients, 35 were treated with fusion and 46 were treated conservatively. Recurrence of the deformity developed in 3 of the 46 patients treated conservatively, and fusion was subsequently done. Thus, a total of 84 cases were analyzed. In the treatment of cervical spine injuries, first consideration must be given to protection of the neural structures. Relieving all pressure from the spinal cord and nerve roots and putting them at rest afford the best opportunity for return of function of the neural structures. To do this with certainty requires accurate reduction of bone structures, followed by internal fixation for immediate stability and spine fusion to prevent late recurrence. The general routine of skeletal traction, internal fixation, and spine fusion constitutes a method of treatment that needs to be varied only slightly in order to be practiced in a large percentage of all serious injuries of the cervical spine.

The results obtained in the 35 spine fusions and in the 46 injuries treated conservatively indicate that the patients in whom fusion was done had less residual deformity and a lower rate of recurrence.

In addition, less time was spent in the hospital or in uncomfortable casts, and less time was spent away from work. The mechanism of injury in fracture-dislocation of the cervical spine is discussed in some detail, with emphasis on the hyperextension fracture-dislocation which is caused by a combination of forcible extension and compression acting from above. A new interpretation of the roentgenologic findings in a large group of fracture-dislocations with mild anterior displacement showed that about 50% of them were caused by hyperextension rather than flexion as previously thought. Before this mechanism was recognized, it was difficult to understand the severe neurological changes that were frequently present. Placing these cases in the group of hyperextension injuries makes the neurological damage understandable.

Brain Abscess. C. V. M. Fog. Danish M. Bull. 5:260-264 (Dec.) 1958 (In English) [Copenhagen].

Fog reviews 114 cases of brain abscess in 89 males and 25 females, representing all age groups. The localization was in the brain stem in only 2 cases, was supratentorial in 11, and was infratentorial in 12. In 33 cases the abscess was otogenic; in 6, rhinogenic; and in 28, thoracogenic. In 11 cases it was due to cranial injuries, in 36 to other causes. The most frequent cause was infection from the ears and nose; the next most frequent cause, infection from the lungs. The bacterium most often found in cultures from pus was Staphylococcus aureus. The mortality was highest in cases with brain abscess of thoracogenic origin. The prognosis is best for sterile abscesses and least favorable in cases with streptococci. Diagnosis may be difficult. A brain abscess may be present without demonstrable leukocytosis or choked disk. Most of the patients were treated by total excision, which was usually preferable to more conservative methods. The mortality has fallen steadily since the advent of penicillin and the introduction of rational chemotherapy, with resistance determinations as a guide in the choice among streptomycin, tetracyclines, chloramphenicol, sulfonamides, and penicillin, but it is still about 25%. Fifty-five of the 59 survivors were followed up. Six had died of other diseases. In the remaining 49, the late prognosis was found to be best for the infratentorial cases. Almost half of the patients with supratentorial abscesses had reduced working capacity.

Experience with Arterial Replacement. H. W. Scott Jr., J. A. Kirtley, R. I. Carlson and J. H. Foster. J. Tennessee M. A. 52:1-3 (Jan.) 1959 [Nashville].

The authors report on 183 patients with vascular disease on whom arterial grafting was performed at the Vanderbilt University Hospital and the Thayer Veterans Administration Hospital in Nashville, Tenn., since 1954. A freeze-dried homologous homograft was employed in 149 patients, and a synthetic prosthesis in 34. Arteriosclerotic aneurysm of the abdominal aorta and arteriosclerotic occlusive disease of the terminal aorta were the 2 commonest indications for arterial grafting in the group of 149 patients; 21 of them died, representing a mortality rate of 14.5%. Segmental arteriosclerotic occlusion of a peripheral artery was the commonest indication for grafting in the group of 34 patients; 4 of them died, representing a mortality rate of 12%.

All the abdominal aneurysms in this series originated below the renal arteries and allowed anastomosis of the grafts, after resection of the aneurysm, without encroachment on the renal vessels. In many of the patients with arteriosclerotic occlusion of the terminal aorta (Leriche's syndrome), blood flow to the extremities was improved by employing bypass grafts from the aorta to the femoral arteries without disturbing collateral vessels in the region of the aortic bifurcation. Bypass grafts were also employed for segmental occlusions of the femoral artery. In other arterial lesions, resection and restoration of normal circulation were performed by graft implantation. The patients were followed for periods of up to 4½ years. The results were good. There was no recurrence of symptoms, and there was good maintenance of function. The incidence of thrombosis in grafts was low (5% in the group with homografts and about 10% in that with synthetic prostheses), and there was no evidence of aneurysmal dilatation of any grafts. Aortograms performed as late as 3 years after graft implantation showed maintenance of structural integrity of the arterial substance. While freeze-dried arterial homografts have functioned well, it is likely that the improved synthetic prostheses curently available will largely replace the homografts as arterial substitutes.

Prognosis in Lung Cancer Surgery Based on Blood Vessel Invasion. E.-D. Gagnon and C. Gelinas-Mackay. Canad. J. Surg. 2:156-160 (Jan.) 1959 [Toronto].

At Notre-Dame Hospital in Montreal during the 9 years from 1949 to 1957, a total of 329 cases of lung cancer were diagnosed, of which 254 were histologically verified by bronchoscopic examination, biopsy of lymph nodes, thoracotomy, or autopsy. In only 77 (30%) of the verified cases was a surgical attempt at cure possible. Of the 77 patients, only 48 could undergo resection. Eleven of these died within 30 days after surgery, leaving 37 who could be followed up. The surgical specimens of these 37 survivors were studied, special attention being given to the invasion of the blood vessels. All patients surviving and "well" for more than 2 years had no blood vessel invasion in the removed lung, and patients dying of other causes likewise had no blood vessel invasion. However, all but one of the patients dying of metastases had blood vessel invasion.

The obliteration of lung vessels by proliferation of the intima seems to be an effective barrier against metastases. The histological type of the carcinoma does not seem to influence the prognosis directly. The presence or absence of blood vessel invasion, more than any other criterion, seems to be important in the prognosis of lung cancer. More attention should be paid to this as an aid to prognosis. Operation at the earliest possible time affords the only chance of cure.

Carcinoma of the Stomach: Follow-Up Investigation in 451 Cases. M. Andreassen. Danish M. Bull. 5:264-268 (Dec.) 1958 (In English) [Copenhagen].

The material comprises 451 cases of carcinoma of the stomach in 319 men and 132 women who were treated from 1945 to 1955 in the Rigshospitalet, Copenhagen. The disease occurred predominantly in the 5th and 6th decades of life. Four patients were under 30 years of age; in such cases the prognosis is usually less favorable, because at this early age the diagnosis of cancer is often overlooked. Only 40 patients sought treatment within 3 months after the development of symptoms. Radical operation was performed in 211 cases, or 47%, with a 3-year survival rate of 21%. The author stresses the importance, in surgical treatment of cancer of the stomach, of more extensive employment of histological examination of the edges of the resection during the operation, with meticulous removal of the lymph nodes and fat from the stomach bed, especially from the hepatic pedicle. Possibly total gastrectomy can be employed to a greater extent if supplemented by an intestinal reservoir introduced between the esophagus and the stomach. Increased palliative resection is recommended in cases in which the tumor cannot be removed radically.

A Contribution to the Knowledge of Saint's Triad (Hiatal Hernia, Gallstones, and Diverticulosis). E. Fedele and L. Sabatini. Policlinico (sez. chir.) 65:243-253 (Oct.) 1958 (In Italian) [Rome].

The authors report on 2 women, 44 and 52 years of age, with Saint's Triad, who were observed at the surgery clinic of the University of Rome during one year. The first patient 4 years before observation felt some pain in the epigastric region. This symptom became more intense and more frequent. No direct relationship between the pain and the digestion was apparent. The patient complained also of a burning sensation in the retrosternal region, which became more severe during hiccups. Difficulty in the digestion of especially fatty foods occurred 2 years before observation; half an hour to 2 or 3 hours after meals the patient suffered pain which originated in the epigastrium and extended to the right of the hypochondrium. One year before observation occasional diarrhea, with semiliquid feces at times mixed with mucus, was noted. Roentgenologic examination showed a hiatal hernia of the sliding type at the fundus of the stomach, and diverticula were seen in the cecum, in the transverse colon, and at the hepatic flexure of the colon. Cholecystography showed 2 transparent calculi at the fundus of the gallbladder. The second patient complained of pain, vomiting, and, rarely, some fever for 14 years before coming to the clinic; these symptoms became more frequent with time. Two years before observation she suffered a sensation of burning in the retrosternal region. Over the years she had made frequent use of laxatives. A large swelling could be felt in the iliac fossa on the right. Roentgenologic examination showed a gastroesophageal reflux; the lower part of the stomach appeared partially herniated through the esophageal hiatus. A mass, the size of a big orange, was noted in the small intestine. Diverticula were seen in the ascending and the transverse colon, and gallstones were noted in the gallbladder.

The authors think that what is usually referred to as Saint's Triad is a syndrome, and that the presence of the 3 pathological manifestations (hiatal hernia, gallstones, and diverticulosis) is a mere coincidence and is not due to a common cause. The association and the interrelation of the manifestations are worthy of investigation in order to remove the lesion which is most responsible for the syndrome.

GYNECOLOGY & OBSTETRICS

Exchange Transfusion in Treatment of Septic Toxemia Due to Clostridium Perfringens. G. Villavicencio G., A. Hille and C. Paredes. Obst. y ginec. latino-am. 16:255-265 (July-Aug.) 1958 (In Spanish) [Buenos Aires].

Eight women with septic toxemia due to Clostridium perfringens after an induced abortion were observed during 1957-1958 at the San Borja Maternity Hospital of Santiago, Chile. The patients were hospitalized 48 to 96 hours after the induced abortion. They were in acute shock (2 being in a condition of irreversible shock), with severe hemolytic anemia, marked hemoglobinemia and hemoglobinuria, jaundice, and uremia with marked oliguria or anuria. During the first day of hospitalization the patients were treated by curettage and administration of antibiotics and perfringens antitoxin, and received a direct transfusion of from 8 to 10 liters of fresh blood. The technique was the same as that used in an indirect transfusion with fresh blood, the injection being given into the cephalic or the jugular vein. Uremia, creatinemia, and uricemia diminished in 2 or 3 days, and diuresis reappeared after the first exchange blood transfusion in 3 out of 5 patients. In the other 2 patients a second transfusion of the same quantity of fresh blood was necessary 4 days after the first for obtaining satisfactory results. One patient had 3 such transfusions during a 24-day period of anuria; diuresis reappeared after the third and last transfusion. The results show recovery of the patients in 75% of the cases. The authors conclude that exchange blood transfusion should constitute a routine treatment of septic toxemia due to perfringens after an induced abortion, being given at the same time that antibiotics and perfringens antitoxin are.

Fluoxymesterone (Halotestin) in the Treatment of Advanced Breast Cancer. K. B. Olson. New York J. Med. 59:248-252 (Jan. 15) 1959 [New York].

Fifteen women, between the ages of 39 and 72 years, with advanced cancer of the breast, were treated with a new halogenated corticosteroid, fluoxymesterone (Halotestin). Thirteen of the 15 patients had previously undergone radical mastectomy, and 8 had been treated previously with either androgens or estrogens. Two patients were premenopausal and had previously been castrated without remission of their disease. One patient was treated on exacerbation of her disease after a remission resulting from hypophysectomy. Fluoxymesterone was initially administered in doses of 10 mg. per day orally. This dose later was increased in all patients to 20 mg. daily. Subjective improvement of some degree, consisting of a sense of well-being, increase of appetite, and a decrease of pain, occurred in 6 patients. Objective improvement, as measured by healing of skeletal lesions and reduction of the size of lymph nodes by more than 50%, occurred in 4 of these 6 patients. The patient who previously had a hypophysectomy had a short objective remission. The 2 menstruating patients who failed to respond to surgical castration likewise failed to respond to fluoxymesterone therapy. Eight patients received no benefit from fluoxymesterone therapy, and all of them subsequently died. Two of the 4 patients with objective improvement died. The usual effects of androgenic hormones were noted in most of the patients continuing therapy for more than one month, as evidenced by hirsutism, acne, increased libido, edema, and increased erythropoiesis, but the impression was gained that these effects were slower to occur and were not of such magnitude as those with testosterone propionate and methyltestosterone.

Fluoxymesterone appears to be a potent androgen and capable of producing objective remission in advanced breast cancer. It has the advantage of being administered orally and is well tolerated in effective doses. It is not known whether doses of more than 20 mg. per day will be more effective, but no remissions were noted with doses lower than that amount. It seems probable that fluoxymesterone is at least as good as other effective androgens and deserves further trial.

PEDIATRICS

Phenylketonuria: An Unusual Case. S. A. Leonard and F. L. McGuire. J. Pediat. 54:210-214 (Feb.) 1959 [St. Louis].

The authors report on an 8¼-year-old girl with phenylketonuria. Physically the child was relatively normal except for her height (47½ in. [120 cm]), which was below the 16th percentile; her weight was normal. Psychological evaluation revealed an intelligence quotient of 70, which would place her within the borderline mental deficient category. Her serum phenylalanine level was 36.5 mg. per 100 cc. and thus did not correlate with her IQ. A routine ferric chloride test gave positive results. The child was found high in ability for rote memory, and it was felt that increased mental age might be obtained with continued environmental security. She was not treated with low-phenylalanine diet because of poor experimental results in older children; in addition, she was asymptomatic. A brief review of the literature showed that the first descriptions of phenylketonuria were all those of severe mental retardation. Psychologically this child was found to be a "phenylketonuric" and not a "phenylpyruvic oligophrenic." The authors believe that "phenylpyruvic oligophrenia" is no longer a correct term for the syndrome of phenlyketonuria, and that the report of this patient may add stimulus to the broadening of the spectrum of phenylketonuria.

Thyroid Cancer in Children. J. R. Moore and A. D. McKenzie. Canad. J. Surg. 2:175-179 (Jan.) 1959 [Toronto].

The authors present the histories of 6 children with thyroid carcinoma, who were observed in the Vancouver area between 1952 and 1957 inclusive. Malignant thyroid tumors in adults were likewise reviewed, and it was found that children accounted for 5% of the group. The children ranged in age from 7 to 17 years, and all but one were boys. That thyroid carcinoma in children is not readily suspected is proved by the fact that in 4 of the children symptoms had been present for from 5 to 18 months. The other 2 children had symptoms for one month each. The finding of a thyroid nodule or nodules in children is more serious than in an adult, and the majority are likely to be carcinoma. It can be expected that the presence of masses in the neck will be the initial sign. As with papillary carcinoma in adults, a considerable number of children will have metastatic lymph node involvement when they are first seen. There were 4 such patients in this series, and one of these had lymph node enlargement as the only clinically demonstrable lesion. Only 2 of the 6 patients had localized thyroid nodules, both on clinical examination and at operation.

Histologically, 5 patients had a papillary adenocarcinoma, while the remaining patient had a papillary follicular type of lesion. Since 1950 there have been several reports on previous irradiation in children who later developed cancer of the thyroid. All 6 of the patients in this series had received irradiation for an "enlarged thymus gland" during infancy. The total dosage in each instance was about 500 r. Surgical excision was the primary treatment in all the patients. External irradiation was used in 2 patients, in one of whom local removal was not complete. Radioiodine (I^{131}) was helpful in one patient. The 2 children with the localized disease are well with no clinical evidence of recurrence, one after 5 years. Residual or recurrent disease is present in the other 4 patients.

A Contribution to the Knowledge of the Christmas Factor Deficiency in Infants. W. Felici and V. Bacchetta. Minerva pediat. 10:1226-1234 (Nov. 3) 1958 (In Italian) [Turin, Italy].

The authors discuss the histories of 2 children with deficiency of the plasma thromboplastic component (Christmas factor). The first child, at the age of 3½ years, had developed a swelling of the left knee because of a fall. The swelling persisted unchanged and painful for 25 days. During the following 2 years the condition improved only upon immobilization of the joint and returned to the initial state whenever attempts to move the knee were made. The child was brought to the hospital at the age of 6, and a diagnosis of hemophilia was made. One month before the last observation he had suffered a gingival hemorrhage. Moreover, owing to trauma to the left gluteal region incurred in a fall, he had developed a hematoma in the same region, with pain radiating into the thigh and the left popliteal region; the swelling regressed slowly and disappeared after 20 days. Coagulation tests gave normal results. The authors believe that hemophilia in this patient, who was the only male child in his immediate family, was hereditary. In taking the history it was revealed that a maternal uncle, at the age of 2 years, had had a profuse hemorrhage caused by a lacerated and contused wound on the forehead; later this relative suffered from rheumatism of the major joints and died at the age of 17 of unascertained causes.

The second child, who died after 2 days of life, showed at birth hemorrhage and plasma thromboplastic component (PTC) deficiency associated with prothrombin and factor VII deficiencies. The brothers of the child had not experienced any hemorrhages. The authors believe that in this child the PTC deficiency, combined with a deficiency of prothrombin and factor VII, was to be considered the result of disturbances in the production of coagulation factors of the plasma by the liver. Such disturbances are frequent in the neonatal age. The diagnosis of a hemophilic syndrome was excluded in this case, inasmuch as the PTC deficiency was not the result of a hemophilia-like disease (Christmas disease), which would imply the operation of hereditary influences, but was the result of functional immaturity or parenchymal alterations in the liver.

DERMATOLOGY

Cryoglobulins in the Chronic Lupus Erythematosus. T. Chorazak. Acta dermat.-venereol. 38:322-328 (no. 5) 1958 (In English) [Stockholm].

The author points out that the obscure etiology of the collagen diseases has led to explorations going beyond the dermatological field, being concerned with such factors as the erythrocyte sedimentation rate, the detection of L. E. cells (Hargraves' sign), and the investigation of the protein pattern of the blood serum. Investigators who studied the blood serum proteins by means of paper electrophoresis in dermatological conditions, and particularly in lupus erythematosus, found that there is a reduction in albumin and an increase in globulins, particularly the gamma globulin fraction. Cryoglobulin (Lerner and Watson's term [1947]) for a blood globulin precipitating in serum at a temperature of from 7 to 11 C [44 to 52 F] is also known as the "cold fraction." Even the presence of small amounts of cryoglobulins is pathological and is classified by the author as a paraproteinemia. Earlier investigators had demonstrated that the electrophoretic velocity of cryoglobulins is similar to that of gamma globulins and perhaps of beta globulins or lies between beta and gamma globulins.

The author investigated the presence of cryoglobulins in the serum of patients with chronic lupus erythematosus and found this "cold fraction" in 48 of 72 patients (67%). He regards this as an extremely high percentage, the more so since others, in examining the serums of 40 healthy subjects, never found cryoglobulins, and he himself failed to find them in 12 persons who were healthy or had only minor skin lesions. Practically all the 72 patients showed hyperglobulinemia, particularly of the gamma and less so of the beta fraction. Of 44 patients with hypergammaglobulinemia, 29 had cryoglobulins. Of 27 patients with hyperbetaglobulinemia, only 17 had cryoglobulins. The author feels that the high incidence of cryoglobulinemia in the patients with chronic lupus erythematosus suggests that this factor has some connection with the pathogenesis of the disease; at any rate, the presence of cryoglobulins cannot be regarded as of no importance, because it usually accompanies serious diseases. The site of formation of cryoglobulins is still controversial; some believe they are formed in the liver, and others in the muscles, in the reticuloendothelial system, in the mast cells or the plasma cells.

No correlation could be found between cryoglobulinemia and the severity of lupus erythematosus, although in 7 patients who had hyperglobulinemia, but no cryoglobulins, the local lesions had healed (thin, smooth scars with pigmented borders but without erythema, infiltration, or sealing). The lack of uniformity of the electrophoretic aspects of patients with lupus erythematosus permitted no definite conclusions. Hyperglobulinemia, with high values of gamma and beta fractions, was found to persist both in active lesions and in locally cured ones. Some observations on the patients studied by the author suggested that the cryoglobulins might be connected with the transition from a chronic to an acute form of lupus erythematosus, with increase in body temperatures, superficial ulcerations on hands and feet, pain and edema in the joints. Corticotropin and cortisone have been observed to cause partial or complete disappearance of cryoglobulins, and it is suggested that this mechanism might be responsible for the beneficial effect of these hormones in lupus erythematosus.

Plantar Wart Treatment with Ultrasound. H. Kent. Arch. Phys. Med. 40:15-18 (Jan.) 1959 [Chicago].

This report is concerned with the use of ultrasonic wave lengths in the treatment of plantar warts. The equipment used in all treatments was a Birtcher Ultrasonic Model No. 105-F, having a frequency of 1 megacycle. The transducer or soundhead is able to deliver a total energy of 0.5 to 15 w. The crystal contained in this transducer is 5 sq. cm. in area and is designed to deliver an output of 0.1 to 3 w. of ultrasonic energy per square centimeter. The coupling medium used on all patients was liquid petrolatum (white mineral oil) U. S. P., a low viscosity fluid which also acts as a lubricant, so that all areas of skin are kept in contact. A gentle firm pressure of the soundhead was maintained during treatment and a rotatory motion employed. The duration of treatment was arbitrarily kept to 15 minutes. With this technique, no complaints were received concerning heat effects or pain. On the contrary, when a wart had been painful, almost complete relief was obtained after the first 5 minutes of treatment.

Nine patients were treated. As a rule, single, discrete, recent plantar warts were preferred. Two patients had multiple warts. The frequency of treatments varied from a single to 11 courses. Of the patients described, one had previously been treated with maximum x-ray doses on isolated warts on both feet. The warts were approximately 2 mm. in diameter, circumscribed by fibrous tissue, and only slightly elevated from the surrounding skin. Bunion pads had been employed because the warts were quite painful. Only the lesion on the left foot was treated with ultrasonic waves. The wart on the right foot served as a control. After the 8th dose, the wart appeared to become more elevated. Pain recurred, but after the wart was sanded down with emery paper, comfort was restored. The lesion became smaller until finally a minimal scar remained. Six months later, the treated wart had not recurred, whereas the wart on the untreated foot remained unchanged.

The general results suggest that ultrasonic therapy is nearly always effective in the treatment of plantar warts. Pain is relieved almost immediately, followed by necrosis of the wart. Normal skin is unharmed by the technique. Changes evoked in these warts suggest either a vascular, a molecular, or a viral effect. Advantages of ultrasonic therapy of plantar warts include quick pain relief and the fact that it involves neither paring nor skin destruction nor scarring nor protective pads, that the patient remains ambulatory, that single warts in difficult locations (edge of heel) can be treated, and that recurrences are apparently prevented.

PUBLIC HEALTH

Report on Edinburgh X-Ray Campaign, 1958: Introduction and Community Arrangements: Technical and Administrative Arrangements: Results of Campaign. H. E. Seiler, A. G. Welstead and J. Williamson. Tubercle 39:339-359 (Dec.) 1958 [London].

The authors report on an x-ray campaign conducted in Edinburgh in 1958. A cooperative effort by local authority, local hospital authority, and the central department of health, with the good will and help of local community workers, achieved an 84.4% response of the public to the request to have chest x-rays taken. The technical and administrative arrangements proved adequate but only as a result of detailed previous planning. Four hundred twenty-three new patients with active pulmonary tuberculosis were found. The highest prevvalence of active tuberculosis was in males over 60 years of age (3.30 per 1,000). The over-all prevalence in males was 2.17 and in females 1.01 per 1,000 persons x-rayed. The importance of older men in the epidemiology of tuberculosis has once again been emphasized. It is noteworthy also that in these men the prevalence of carcinoma was as high as 2.34 per 1,000. It is concluded that an x-ray campaign of this sort is a useful and justifiable method of case finding for tuberculosis and other serious chest diseases. It is particularly suitable in communities where tuberculosis appears to be coming satisfactorily under control, and it may advance the day of final conquest of the disease by several years.

BOOK REVIEWS

The Effect of Advancing Age upon the Human Spinal Cord. By L. Raymond Morrison, M.D., with collaboration of Stanley Cobb, M.D., and Walter Bauer, M.D. Cloth. $6. Pp. 127, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E.C.4, England, 1959.

It is regrettable when it is not possible to write a favorable review of a book published posthumously. Unfortunately, this book fails in the purpose for which it was written; the changes in the spinal cord which result from advancing age are not presented in an intelligible manner. The material on which this study was based has been poorly chosen. These spinal cords were taken from the bodies of persons who died from a variety of systemic diseases such as rheumatic heart disease, lupus, ulcerative colitis, lymphoblastoma, and uremia. At least two of the patients had a pyramidal tract lesion, and at least one of these was from cerebral infarction. The reader is not informed as to the cause of death in all of the patients, nor is he given any information by means of which he might discriminate between the anatomic changes produced by aging and those resulting from disease processes. The author does not attempt to make such a differentiation, and one doubts if such could be made with accuracy on this material. It is surprising to learn that "The brains were not examined in this series." Even the changes which were observed have not been organized in a systematic fashion, and no clear-cut picture is presented of the changes produced by advancing age.

The poor sentence structure and unfortunate choice of words are striking. This monograph has been published with the aid of money from a fund established to support scientific research. The lack of a scientific approach to the problem in hand is disturbing. As if to expand a very short text into a book of even this small size, the publisher has resorted to extremely wide margins and to the use of illustrations two and three times as large as they need to be. Only the first 52 pages of this book are devoted to the subject of the title. The rest consists of an atlas of sections, stained by the Weigert and Nissl methods, of a "normal spinal cord" removed from a 24-year-old woman who died of subacute bacterial endocarditis with an occasional focus of abnormality within the spinal cord. The Weigert preparations are in no way unusual, while the sections stained by Nissl's method are reproduced at such a low magnification as to be of little value. There is no index.

Cancer. Volume 2, Part II: Pathology of Malignant Tumours. Volume 3, Part III: Additional Pathological Aspects; Part IV: Geography of Cancer; Part V: Occupational Cancer; Part VI: Cancer Education; Part VII: Cancer Detection. Edited by Ronald W. Raven, O.B.E., T.D., F.R.C.S., Joint Lecturer in Surgery, Westminster Medical School, University of London, London. Cloth. $18 per volume. Pp. 641, 25, with 357 illustrations; 483, 18, with 165 illustrations. Butterworth & Co., Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada, 1958.

Cancer. Volume 4, Part VIII: Clinical Aspects. Edited by Ronald W. Raven, O.B.E., T.D., F.R.C.S. Cloth. $126 per set of 7 volumes. Pp. 532; 23, with 173 illustrations. Butterworth & Co., Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada, 1958.

The first volume of this six-volume British compilation on cancer was reviewed in The Journal of the American Medical Association for March 8, 1958, page 1257. The review was favorable and concluded that every investigator and student of cancer should have access to the work. This opinion is hard to maintain after the examination of these three subsequent volumes. Volumes 2 and 4 deal with human cancer by the major anatomic sites of the neoplasms, volume 2 being on pathology and volume 4 on clinical aspects. This separation is unattractive to this reviewer, particularly since radiotherapy is relegated to the forthcoming volume 5. As a result, for carcinoma of the uterine cervix, pathology is to be found in volume 2, certain clinical features in volume 4, radiotherapy in volume 5, and cytodiagnosis in a section of a chapter in volume 3. The presentation of this and other important human neoplasms becomes choppy, closely interrelated aspects are torn apart, and some important considerations are barely touched on while others are unnecessarily duplicated.

Volumes 2 and 4 are written almost entirely by British authors. In general, the concepts and practices of pathology and of clinical management of cancer do not differ significantly from those of a similar cross-section of authorities who might have been selected in the United States. Differences do appear, however, more related to individual experiences than to national practices. For example, the editor contributes a 20-page chapter on the clinical aspects of breast cancer. The advice regarding treatment is, for clinical stage 1, radical mastectomy and postoperative radiation; for clinical stage 2, preoperative radiation followed by radical mastectomy. "Oophorectomy should be performed for all premenopausal patients . . . irrespective of the stage of disease." These recommendations would not be in agreement with the practices of many other centers. No other views are presented; the recommendations are not supported by

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

the limited statistics on end-results from the Royal Marsden Hospital; and that is all that is said about prognosis. In contrast, one whole page and 4 of 31 references are devoted to adrenalectomy and hypophysectomy, with the prospectus for volume 6 indicating additional separate chapters on each of these subjects.

The first chapter of volume 4 presents the subject of staging and emphasizes a "TNM" system that is still under discussion as a possible standard. It seems odd that no special consideration is given to end-results, survival analysis, or the duration of cancer among "untreated" patients, particularly since Great Britain has been the first to use biometric surveys and has some excellent regional and national cancer registries.

Volume 3 is divided into five main parts, including additional pathological aspects, geography of cancer, occupational cancer, cancer education, and cancer detection. The 23 chapters by 22 authors are of widely different quality, and the collection displays a lack of over-all editorial integration. The chapter on tissue culture is good, but it is directed to the growth of cancer cells, which obscures the recent difficulties in separating "normal" from "neoplastic" cells under conditions of in vitro culture. The chapter on neoplasms in domesticated animals should have been either much longer or much shorter. It has the appearance of editorial dissection, leaving some sections misleading in their incompleteness, and retaining such trivial data as a list of the most popular breeds of dogs in Great Britain and the United States. The best chapters in volume 3 are on the epidemiology of cancer, and this reviewer would have liked to have a whole volume devoted to these studies. The reports by Stocks, Dorn, and Clemmesen are particularly noteworthy, yet nowhere is it made clear that these population-based incidence analyses should not be compared directly with the relative distribution frequency studies from India and South Africa. The excellent chapters on occupational cancer of the skin and urinary bladder and leukemia could well have been extended to include occupational neoplasms of the lung and upper respiratory passages.

Cancer education is treated in chapters that appear to be essentially promotional progress reports of the sponsoring agencies. Only the paper by Wakefield presents the philosophy and the limitations of this field of endeavor. The two chapters on cancer detection, by O'Donnell and Day, are thoughtful, complete descriptions of more than passing value.

These three volumes, it is regretfully concluded, compare badly with several other textbooks on cancer. In the field of research "The Physiopathology of Cancer," edited by Homburger and Fishman, is certainly a more intelligently gathered collection, while for the clinical-pathological aspects "Cancer," by Ackerman and del Regato, retains its place as the best source in English. Knowledge about cancer is so incomplete that anything approaching a systematic compendium is an impossibility. The best that can be done is to collect the views of the recognized leaders in the field, without the illusion that these views are necessarily correct. Under these circumstances it might be desirable to print on the cover of such compilations of cancer data a warning to the reader, such as "Opinions contained herein are those of the authors and do not necessarily reflect the truth, especially when such opinions are presented as facts."

History of the Second World War: United Kingdom Medical Series. Editor-in-chief: Sir Arthur S. MacNalty, K.C.B., M.A., M.D. The Royal Air Force Medical Services. Volume III: Campaigns. Edited by Squadron Leader S. C. Rexford-Welch, M.A., M.R.C.S., L.R.C.P. Cloth. 105 *shillings*. Pp. 730, with illustrations. Her Majesty's Stationery Office, Atlantic House, Holborn Viaduct, London, E. C. 1, England, 1958.

This is the third and final volume of the Royal Air Force portion of the medical history of World War II. The volume consists of 721 pages, containing discussions of the principal campaigns in which the Royal Air Force participated. There are 67 plates, 58 maps, and 37 figures. The medical activities of the RAF are covered in 11 campaigns, extending geographically from the equator to the Arctic Circle. Medical conditions varied greatly, as one would expect, the problems of northern Russia being far different from those of equatorial Africa.

The plans made for continental Europe in 1939 had to be discarded after the destruction of the entire Polish Air Force in the first 48 hours of the invasion of Poland, and it became necessary to disperse all units. At times air squadrons were split up between air fields 30 miles apart, making executive and medical administration difficult. In addition, the weather during the winter of 1939-1940 was severe and temperatures fell at times to below 0 F. The losses due to enemy action from Sept. 3, 1939, to June 19, 1940, totaled 407 deaths and 632 wounded. The average strength during this period was 15,172, with an average number of casualties of over 48 hours' duration of 28.3 per thousand.

The Norwegian expedition was undertaken at short notice with little or no preparation. It was short-lived, however, and lasted only from April 20 to June 8, 1940. The campaign in Libya and Tunisia was a difficult one, operations commencing with the initial Italian advance into Egypt in 1940. Prior to this the RAF had several peacetime garrisons in Egypt with a strength of nearly 6,000. The provision of an adequate water supply in the desert was extremely difficult, due to both scarcity and poor quality. At times the troops were issued water with a saline content of 1,700 ppm. In certain places malaria was endemic. A condition known as "desert sores" was common; these were indolent ulcers of undetermined cause. Dysentery, typhoid, infectious hepatitis, typhus, and relapsing fever all occurred in the command.

It was during the Middle East campaign that air evacuation of sick and wounded was initiated. In March, 1941, the Australian government indicated its willingness to provide, staff, and maintain an air ambulance unit consisting of three converted DH-86 airplanes. Meanwhile, the RAF and the South African Air Force had converted a few airplanes, so that by November, 1941, 8 or 10 air ambulances were available for duty in the Middle East.

In the Greece and Crete campaign (1940-1941) suitable sanitary conditions were difficult to maintain. On Crete the RAF had its first encounter with air-borne troops as the Germans landed about 7,200 men on the first day. This number was augmented later and caused the withdrawal or capture of all British. The 151st RAF wing served in north Russia from September to November of 1941. There was little sickness in this command. Malta, West Africa, Italy and the Balkans, India, and the Far East were also the sites of RAF campaigns as was, of course, continental Europe prior to the liberation. The book is well written and easy to read. The only confusing thing to an American reader is the use of initials instead of complete names of units, installations, and activities. A glossary would prove useful.

Practical Blood Grouping. By F. Stratton, M.D., D.Sc., D.P.H., Director, Blood Transfusion Service, Manchester, and P. H. Renton, M.D., B.Sc., Deputy Director, Blood Transfusion Service, Manchester. Cloth. $9. Pp. 331, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

This is the second book on blood grouping techniques that has been published in England in recent years. This book is more than a dry presentation of methods, since it gives a coherent account of blood group serology, and each point that is made is illustrated by a brief case history. Included in the book are 74 such cases, which enliven the presentation. The usefulness of this excellent review of blood group methodology, however, is seriously impaired by the inclusion of the same misconceptions and mistakes which have stigmatized the literature on blood groups for more than a decade. To mention only a few examples the authors cite with seeming approval the recent numerous investigations purporting to show an association between particular A-B-O groups and disease but fail to mention any of the criticisms which have been leveled against these reports by Wiener, Manuila, and others. The authors again cite as an established fact the highly questionable reports of rises in Rh antibody titers during pregnancy in sensitized Rh-negative women carrying Rh-negative babies.

The report of W. Weiner on the supposed anti-e specificity of autoantibodies tested by him, though poorly documented, has been widely accepted; and the authors of this book claim to have found a similar case of autoantibodies of anti-C+e specificity, although the flimsy evidence presented on page 242 appears to contradict rather than support this conclusion. The claims of anti-e specificity of autoantibodies by many other workers, not including A. S. Wiener, following the original report of W. Weiner, are reminiscent of the unsubstantiated claims of serums of anti-d specificity after Fisher's announcement of his "predictions." Probably, for every dozen reports of autoantibodies of anti-e specificity, there has been at most a single bona fide case.

On page 154, the authors again repeat the myth of the six Rh antigens C, D, E, c, d, and e. Moreover, they write, "Wiener considers that there are 8 alleles at a single locus so that the antigens . . . are determined in threes by a single gene." This is incorrect, since the myth of triple inheritance also was originated by C-D-E adherents. Wiener maintains instead that Rh agglutinogens are each characterized by multiple blood factors, ranging up to 10 factors for certain agglutinogens at the present stage of knowledge, and increasing as new Rh-Hr antibodies are found. The authors also assert that there are in use three different notations for the Rh-Hr types, namely, the C-D-E notations, the Rh-Hr notations, and "the so-called clinical notations much used in Great Britain." However, the so-called clinical or shorthand notations are nothing more than an adaptation of Wiener's Rh-Hr nomenclature, so that there are actually two, not three, nomenclatures in use. Thus, the objection to the Rh-Hr nomenclature being too difficult to understand implies that Wiener's Rh-Hr notations become more understandable only after they are renamed "clinical or shorthand notations."

In view of these faults the book regrettably cannot be recommended to beginners, because it is far more difficult to unlearn incorrect teaching than it is to learn a subject correctly in the first place. Fortunately there are more reliable books available at the present time, with whose aid beginners can readily orient themselves in this complex but important subject.

Clinical Chemistry in Practical Medicine. By C. P. Stewart, D.Sc., Ph.D., Reader in Clinical Chemistry, University of Edinburgh, Edinburgh, and D. M. Dunlop, B.A., M.D., F.R.C.P., Christison Professor of Therapeutics and Clinical Medicine, University of Edinburgh. Fifth edition. Cloth. $6.75. Pp. 342, with 30 illustrations. E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland; [Williams & Wilkins Company, 428 E. Preston St., Baltimore 2], 1958.

The number of editions this short English textbook has gone through suggests that it is a useful book to at least some members of the medical profession. As the title indicates, it is a synopsis of laboratory examinations in clinical medicine. A chapter is devoted to each subdivision (e. g., cerebrospinal fluid and hepatic function), and each chapter consists of a short discussion of basic physiology, followed by a list of the more important tests and the principal changes encountered in disease. The material presented is accurate and up to date, and it is well and simply written, an almost universal virtue of English textbooks. The only defect of this book is its brevity; it is too synoptic. Too much has been left out, and what is presented is given in too short a manner to make it effective. For example, 14 pages are devoted to the basal metabolic rate. Three or four sentences are given to protein-bound iodine (PBI), and the subject is then dismissed with the remark that it is not suitable for routine work. In listing the causes of low glucose concentration in the spinal fluid, no mention is made of diffuse meningeal carcinomatosis. In the chapter on hormone abnormalities almost nothing is said of normal or pathological blood and urine values for the hydroxycorticosteroids, although three pages are given to the 17-ketosteroids. This book is not suitable for medical students or for physicians who want a thorough knowledge of the subject. It will certainly be useful to students of biology and biochemistry and will probably prove satisfactory for candidates for professional examinations who want a quick review of a very important subject.

Occupational Allergy: Lectures Held During a Course on Occupational Allergy at The Hague in May, 1958, Organized by the Netherlands Society of Allergy in Co-operation with the Netherlands Institute for Preventive Medicine and the Netherlands Society of Occupational Medicine Under the Auspices of the European Academy of Allergy. Cloth. $10. Pp. 329, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; H. E. Stenfert Kroese N. V., Leiden, Netherlands, 1958.

About 40 authors, including allergists, internists, pediatricians, rhinologists, and dermatologists, among others, contributed to this volume. Essentially, the book discusses various allergic manifestations produced by occupational duties, methods of allergic examination, diseases and their causes in the various professions and industries, therapy, prophylaxis, and socioeconomic aspects. Among the occupations discussed are those of wool textile workers, bakers, printers, nurses, wood workers, cement workers, miners, and employees in pharmaceutical industries. While the material is informative and may be helpful to European physicians, it is inadequate for the American physician, who is faced with problems involving plastic, petroleum, rubber, and all the complexities of a variety of chemical industries. The book lacks organization, as shown by an unevenness in the different contributions as to the factual material, form of presentation, and form of references (presence or absence of references, with or without titles, last name or first name first, full name or initials, and many errors in the spelling of names). Despite imperfections this volume can serve as a supplement to a library on occupational allergy.

Handbook of Histopathological Technique (Including Museum Technique). By C. F. A. Culling, F.I.M.L.T., F.R.M.S., Chief Technician, Westminster School of Medicine, University of London, London. With foreword by R. J. V. Pulvertaft, O.B.E., M.D., F.R.C.P. Cloth. $9; 45 shillings. Pp. 446; 27, with 80 illustrations. Butterworth & Co., Ltd., 88 Kingsway, London, W. C. 2, England; 1367 Danforth Ave., Toronto 6, Canada, 1957.

To write a handbook of histopathological technique is a difficult undertaking, in this time of rapid advances. The author has composed a remarkably inclusive book based on his many years of extensive experience in this field. The work is devoted essentially to the fundamentals of histopathological technique, and the author does not attempt to cover many of the procedures involved in histochemistry. Of particular importance, and not covered in other existing works of this kind, is a section on museum technique. Another section deals with the microscope and various aspects of microscopy, including fluorescent microscopy, polarizing microscopy, and phase-contrast microscopy. The author has produced an excellent coverage of the fundamentals of histopathological technique. His emphasis on fundamentals, with the purposeful exclusion of many techniques in histochemistry, has added to the value of this work, which should prove extremely helpful to the student.

Problems of Addiction and Habituation. Edited by Paul H. Hoch, M.D., and Joseph Zubin, Ph.D. Proceedings of forty-seventh annual meeting of the American Psychopathological Association, held in New York, February, 1957. Cloth. $6.50. Pp. 250, with 12 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England. 1958.

This book consists of 15 articles and 2 discussions by various authors. Most of the articles review work already published elsewhere. The subjects of various articles cover a wide range, from the development of experimental neuroses in animals to the factors relative to social and psychiatric management of addiction in the United States. Tiebout makes an eloquent plea for direct treatment of the symptom of alcoholism; Masserman attempts to review an enormous mass of work on the effects of drugs on various forms of behavior in animals; Speer defends the use of severely repressive legal measures in the management of narcotic addiction; while Bowman favors a permissive system for the management of addiction in the United States, similar to the plan developed by the New York Academy of Medicine. As might be expected, the quality of the various articles is uneven. The book should be of most value to persons working with the problem of alcoholism or drug addiction.

QUESTIONS AND ANSWERS

ESTROGENS AND CLOTTING

To the Editor:—*If estrogens are given intravenously to control hemorrhage by quickly increasing the concentration of prothrombin and accelerator globin, is it not reasonable to expect similar action, to a lesser degree, when they are taken orally? If this is so, would there not be a greater possibility of arterial occlusion, particularly coronary, among the rank and file of women who are taking estrogens?*

M.D., California.

Answer.—The changes observed in the blood components that promote coagulation accompany the intravenous injection of relatively large amounts of the conjugated estrogens. This rapid increase in the estrogens seems to be essential. The continued oral administration, with slower gastrointestinal absorption, apparently does not have the same effect. Ancillary changes in capillary integrity, circulating lipids, and other elements involved in coagulation accompanying estrogen administration possibly protect the vascular system from the increased coagulability of the blood. Such an "explanation" for the lack of vascular disease in women taking estrogens is at present without complete experimental foundation. It is, however, known that purified components of the conjugated estrogens do not give rise to the same changes in coagulation components or to as great a degree if change does occur.

OPTIMUM HUMIDITY

To the Editor:—*What range of humidity is considered best for skin and mucous membranes? Has air-conditioning been known to reduce humidity to the point of inducing dermal or mucosal irritation?*

James H. Lade, M.D., Albany, N. Y.

Answer.—There are not sufficient scientific data at present to determine the humidity which is best for the skin and mucous membranes. Excessively low humidity, 20% or lower, causes drying of the skin and mucosa with decreased activity of the cilia lining the upper respiratory tract. Excessively high humidity may give an uncomfortable sensation and in warm weather interferes with heat loss. In cold weather any type of heating system or air-conditioning without accompanying humidification may give a low humidity, but any irritation of the skin and mucosa would be due entirely to the drying effect. In warm weather low humidity is not likely to occur with air-conditioning because dehumidification is expensive.

FUEL OIL DERMATITIS AND SEQUELAE

To the Editor:—*A 35-year-old pregnant woman, finding her basement floor flooded with fuel oil which had escaped from the tank, removed her hose and shoes and waded across the floor to turn off the valve and then proceeded, still barefoot, to clean up the basement. During the night she developed a massive macular eruption on her feet and ankles which was pruritic and burning. The next morning she discovered that she was unable to void, and she did not void until catheterization was done in the mid-morning. The urine at that time was almost milky in color and contained a few red blood cells, much mucus, many casts, and many leukocytes. After this she voided with difficulty because of tenesmus and dysuria which persisted until medication, which had been prescribed, became effective within 24 hours. Six days later she began to develop lower abdominal cramps which she said were like mild labor pains. In 48 hours she began to show some spotty uterine bleeding, and at the end of five days she had an abortion of an 8-week-old fetus. It is thought that the dermatitis was due to contact with the fuel oil and assumed that the urinary symptoms were due to the absorption or inhalation of some of the hydrocarbons in the fuel oil. May it be said that the abortion was also due to the toxic effects of the fuel oil?*

L. Mason Lyons, M.D., Terre Haute, Ind.

Answer.—In general, it can be said that there are no components of fuel oil which will cause all of the pathological changes observed in this patient. The occurrence of dermatitis after contact with fuel oil and its specific localization to the exposed portions of the body is rather conclusive evidence that some constituent of the fuel oil was the etiological agent, although two factors—the "massive macular eruption" and its appearance almost immediately after exposure—are not characteristic

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

of the usual dermatitides due to fuel oil. The patient's symptoms and urinary findings present a confused picture: the tenesmus, dysuria, mucus, and cellular elements indicate a cystitis, whereas the many casts show some renal involvement. The milky color of the urine requires more data for explanation, and no information is given regarding a febrile reaction or the presence of systemic symptoms. An abortion occurred one to two weeks after exposure and supposedly after all the dermal and urinary manifestations had subsided. No other associated systemic symptoms are given. Apparently this patient had no signs or symptoms referable to the central nervous, respiratory, or gastrointestinal systems, and some would certainly be expected if there had been inhalation of a volatile material or absorption through the skin of almost any known toxin. The components of fuel oil are not known to cause any of the pathological changes in the urinary or genital tract which occurred in this patient, nor is there any additive or solvent which would produce them. Therefore, while it seems more than likely that the dermatitis was due to the fuel oil, the rest of the patient's difficulties cannot be explained on the same basis and it is not clear why they occurred.

SIDE ACHE

To the Editor:—*What is the cause of the pain commonly experienced in the flank or upper part of the abdomen during strenuous exercise or rapid walking? An 18-year-old boy is unable to play basketball because of pain in the upper part of the abdomen which occurs only during exertion and which is relieved promptly by rest. Studies, including electrocardiogram, complete gastrointestinal series, and sickle cell preparations, all give negative findings. What treatment is recommended?*

M.D., Kentucky.

Answer.—The differential diagnosis of stabbing pains in the chest was considered by Langley (*Ann. West. Med. & Surg.* 6:49, 1952). He listed a number of conditions in the thoracic viscera, thoracic wall, vertebral column, and abdominal viscera and mentioned the common "stitch in the side" or "side ache" about which many young people complain when running. He ascribed it to "strain of an intercostal muscle," but this explanation is given without evidence. Observations on 114 attacks of side ache in 55 persons were reported by Capps (*J. A. M. A.* **116**:2431 [May 24] 1941). The important features were found to be a constant relation to exertion, a tendency for the ache to occur after eating, a variable location, usually in either the right or the left upper quadrant of the abdomen, relief by bending over or from local pressure, and a tendency to aggravation in cold weather. Previously proposed theories regarding the mechanism of pain are untenable. Anoxemia of the diaphragmatic muscle for the side ache is the explanation offered. Why the pain is unilateral is not clear. Perhaps the person stops exercising before the other side begins to hurt. Improved breathing might well put less of a load on the diaphragm. There are theoretical reasons for supposing that recently introduced muscle-relaxant drugs might reduce the tendency of the diaphragm and intercostal muscles to go into spasms and that one or another of the many vasodilators now available might prevent ischemic contractions of these muscles. As yet, however, no studies along these lines have appeared.

INFECTIOUS HEPATITIS AND PREGNANCY

To the Editor:—*Are pregnant women less susceptible to infectious hepatitis than the rest of the population? Is this disease more benign in pregnant as compared to nonpregnant women? If pregnant women are not less susceptible to infectious hepatitis, should they receive gamma globulin for their own protection and for the protection of the fetus?*

Bertrand M. Bell, M.D., Donaldson, S. C.

Answer.—There is no evidence that pregnant women are less susceptible to infectious hepatitis than the rest of the population. Pregnancy places a greater strain on the liver, and infectious hepatitis in pregnancy is more dangerous not only for the mother but also for the fetus. If pregnant women are exposed to infectious hepatitis, gamma globulin should be given for protection of both mother and fetus. An intramuscular injection of about 0.02 ml. per pound of body weight would be suitable.

BLOOD SUGAR DETERMINATIONS

To the Editor:—*A newly employed, well-trained, registered technician has insisted on the use of what is called the dextrose-kit method of performing the blood sugar test. He maintains that this is as accurate as the older Folin-Wu method. Is he right?*

M.D., Alabama.

Answer.—The answer to this problem depends to a certain extent on which dextrose-kit method is used. There are several so-called dextrose-kit methods in which no colorimeter is required. The final color in the blood test is compared with color standards until a match is obtained. For example, one such test is based on the ferricyanide method of Folin. Color standards are set up in milligrams per 100 cc., and the results are accurate within about 10 mg. per 100 cc. of blood. Another method is based on the reduction of copper sulfate (Folin). The resulting color is matched against a color scale with 50-mg. intervals. The colors are much like those produced with Benedict's solution when used to test the urine for sugar. With this method, there is a wide range in the accuracy of the reading. With any of these tests, no appreciable time is saved as compared with the standard blood sugar methods with use of a regular colorimeter. With all these methods, the blood needs to be precipitated and filtered. The filtrate, when mixed with the appropriate chemicals, is boiled for a given period. Consequently, no appreciable time is saved. Any physician who employs a medical technician should use a standard method with a regular colorimeter to obtain an accurate blood sugar level reading.

KOILONYCHIA

To THE EDITOR:—*What is the treatment of koilonychia which has developed spontaneously in a 63-year-old woman? She first developed spooning of her fingernails two years ago, and it has progressed to involve all of the fingernails and has begun to involve the toenails as well. She has taken gelatin faithfully for over a year without any effect. Even though she was not anemic iron was given by mouth, without benefit. In the hope of producing some favorable effect, one physician prescribed large doses of the vitamins A, B, and C, as well as calcium tablets. These agents were given for three months, and no improvement was noted. The patient's basal metabolic rate and plasma cholesterol level are normal. Are any systemic diseases known to be associated with this condition?*

M.D., Ohio.

ANSWER.—Koilonychia still remains a real therapeutic problem in many instances. It may affect several fingers or all fingers at the same time, though very rarely. While it is common in some families, in others it occurs individually. It has been found to coexist with lichen planus, occasionally with other rare skin diseases, in extreme cachexia, and, rarely, with syphilis. On the other hand, it is often difficult, if not impossible, to determine the etiological agent. Several observers, such as Cipollaro, believe that many of these are occupational in origin, i. e., that they result from handling strong acids and alkalies, but others have not found this to be an important factor. A few cases have been associated with dystrophy of the hair and plantar and palmar hyperkeratoses. In some of these patients, vitamins A and D and calcium have been of help. In a few patients there has been an achlorhydric anemia which responded to appropriate iron medication, but there appears to be no such connection in the case in question. In this instance, apparently no cutaneous or internal abnormalities have been found. It would be justifiable to use vitamin D and calcium salts, the latter in the form of calcium gluconate given intramuscularly.

HYPERSENSITIVE DENTIN

To THE EDITOR:—*About a year ago, information was obtained for the treatment of hypersensitive dentin. This included use of ammoniated silver nitrate, followed by 1 drop of eugenol, and brushing the teeth with hot mineral oil, Andresen's paste, sodium silicofluoride, or Thermodent tooth paste. A sodium fluoride-kaolin-glycerin mixture and stannous fluoride were not recommended because they might cause degeneration of the dental pulp. Is any other treatment recommended?* *M.D., West Virginia.*

ANSWER.—All methods named have their enthusiastic proponents, but controlled clinical studies to support them are generally lacking. The sodium fluoride-kaolin-glycerin mixture has been adequately tested and shown to be an effective desensitizer. It can be used safely because damage to pulp results only when sodium fluoride is used in freshly cut cavities and, therefore, does not apply to desensitizing applications. Except for the fact that stannous fluoride and silver nitrate may stain teeth, they are perfectly safe. Desensitizing agents will not prevent recurrence of sensitivity if erosion is continuing and exposing fresh, sensitive dentin. Treatment should include correction of factors causing erosion or gingival caries. Andresen's paste, which is a mixture of phosphates and other salts, for daily application, is supposed to do this, but the evidence is unconvincing.

PHENOL FOR RHEUMATISM

To THE EDITOR:—*Many people in this area use phenol as a sort of home remedy in the treatment of rheumatism, arthritis, and allied diseases. The usual dose is one drop, diluted with water, taken three times a day. Good results are claimed. Would this be safe over a prolonged period?*

M.D., Missouri.

ANSWER.—There appears to be no therapeutic rationale for the administration by mouth of phenol in any form of arthritis. This consultant would advise against it.

"AIR PLATES" AND CONTROL OF HOSPITAL INFECTIONS

To THE EDITOR:—*A more satisfying answer to the question on "air plates" and control of hospital infections, published in* THE JOURNAL, *Dec. 27, 1958, page 2329, can be found by perusal of the book by Wells (Airborne Contagion and Air Hygiene, Cambridge, Mass., Harvard University Press, 1955). Briefly, a 15-minute exposure of a Petri dish represents the number of particles settling out on 1 sq. ft. per minute (rate of deposit). Volume air samplers collect the total number of bacteria in a given volume (bacterial* *density). Settling velocity is the quotient. A high settling velocity (greater than 1) indicates dustborne bacteria and a low velocity, droplet nuclei (less than 4 ft. per minute). Room air has a settling velocity of 1 or 2 ft. per minute, indicating the preponderance of dustborne organisms. Settling velocities can be used to differentiate airborne from dustborne contagion.*

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AEROPHAGIA

To the Editor:—*In* The Journal, *Nov. 22, 1958, page 1734, in answer to a question on aerophagia the consultant suggested eating with the mouth closed as a preventive measure. While it is true that this may help, much of the swallowed air enters the esophagus through the nose rather than the mouth. To prevent this, some form of nasal pinchers, such as those used in underwater training of lifeguards, would be helpful, or small cotton pledgets moistened with water might be placed in each nostril. Charcoal is of doubtful value because a very large quantity would be required to absorb all the air in the stomach. Furthermore, charcoal loses its ability to absorb gases when it is wet.*

G. Franco Capuani, M.D.
Bal. Lamarmora, 15
Novara, Italy.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*It will rarely be necessary for persons with aerophagia to use pinchers or pledgets of moist cotton to close their nose when swallowing. This would be quite impractical, if not impossible. Furthermore, when the nose is closed, a person takes in air through his mouth. It is not clear just how charcoal works in a situation like this. From our clinical experience, however, it definitely reduces the amount of intestinal gas and it has been thought to do so by absorption. Many persons get striking relief from gaseous dyspepsia by this simple procedure.*

URIC ACID AND PREECLAMPSIA

To the Editor:—*In regard to the question on uric acid and preeclampsia, which appeared in* The Journal, *Feb. 14, 1959, page 777, it may be relevant to point out that chlorothiazide may raise the serum uric acid level (Laragh and others,* J. A. M. A. 166:*145-152 [Jan. 11] 1958; Oren and others,* J. A. M. A. 168:*2128-2129 [Dec. 20] 1958). Chlorothiazide is often given to patients with toxemia of pregnancy. Currently, at Cook County Hospital, work being done on this subject seems to indicate that when chlorothiazide is given in doses of 0.5 Gm. twice daily a slight increase in the serum uric acid level occurs in pregnant patients with and without toxemia. Perhaps the inquiring physician used larger doses. The hyperuricemic effect of chlorothiazide may be important if one relies on the uric acid level for prognosis or treatment.*

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Chicago 25.

BLOOD PRESSURE DETERMINATION AND VALVULAR DISEASE OF THE HEART

To the Editor:—*In the Jan. 10, 1959, issue of* The Journal, *page 202, a question appeared concerning the "sea gull murmur," described as a high-pitched systolic murmur; the consultant indicated this is a "high-pitched, screeching systolic murmur maximal near the cardiac apex." The information which is available to me on this subject is somewhat at variance with these opinions. According to Groom and Boone (*Ann. Int. Med. *42:1214, 1955), the sea gull murmur, also known as the "dove-coo" murmur, is a unique musical murmur, decrescendo in character, prolonged through most of diastole, and generally maximal in the mid-precordium. The consultant indicated that most of these murmurs have been shown to be associated with eversion or retroversion of an aortic valve cusp, usually from syphilitic aortitis.*

George X. Trimble, M.D.
Seaside Memorial Hospital
1401 Chestnut Ave.
Long Beach, Calif.

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The comment relative to the sea gull murmur is appropriate if it is based on the article by Groom and Boone, because in that article the sea gull murmur is described as synonymous with the dove-coo murmur. This consultant knows of no authoritative source to indicate that a sea gull murmur has specific diagnostic value. By common usage it has come to mean a high-pitched, musical, screeching murmur, and most of these are systolic in time, in contrast to a similar musical murmur, diastolic in time, which may be specifically related to aortic insufficiency. This seems to be a matter of semantics which does not have a firm traditional foundation.*

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TRANSFUSION REACTIONS AND THEIR TREATMENT, ESPECIALLY WITH THE ARTIFICIAL KIDNEY

Gurbuz M. Barlas, M.D.
and
Willem J. Kolff, M.D., Cleveland

Transfusions of incompatible blood caused severe reactions in 16 patients; 13 cases are described. The usual course consisted of three successive periods referred to as the acute, the oliguric, and the diuretic phases. In the acute phase many of the characteristic symptoms may be masked by anesthesia; watchfulness is therefore necessary, and recognition of symptoms has to be followed at once by cessation of the transfusion and treatment for shock. In the oliguric phase it was necessary to be on guard against overhydration, edema, hypertension, hyperpotassemia, acidosis, uremia, and infection (especially bronchopneumonia). Twelve of the patients in this series were treated with an artificial kidney and nine recovered. In six of them recovery would have been very difficult or impossible without the hemodialysis.

MUCH has been written about unusual causes for transfusion reactions—allergies,[1] pyrogens,[2] and rare blood groups[3]—but there is an understandable reluctance to write about the most common cause of trouble, simple incompatibility or mismatching of blood. Still, transfusion of incompatible blood is the cause of most so-called transfusion reactions; its occurrence is not rare. This paper outlines the treatment and reports our experiences, especially with dialysis, in the treatment of the acute renal failure that follows transfusion of incompatible blood.

Clinical Phases After a Transfusion Accident

It is convenient to consider three phases in acute renal failure: (1) acute reaction, (2) oliguric phase, and (3) diuretic phase.

Acute Reaction Phase.—Symptoms and signs of acute transfusion reactions can be listed as follows, but it should be remembered that anesthesia masks most of the symptoms: chill followed by fever, pain in the lumbar region, flushing of the face or cyanosis, substernal pain, headache, anxiety, nausea and vomiting, cough, rapid and shallow breathing, and distention of neck veins.

There may be symptoms of shock: hypotension, tachycardia, collapse, or prostration. Hemoglobinemia can be found if a blood sample is drawn and centrifuged within an hour or two after the accident. Jaundice usually follows and becomes evident in 3 to 24 hours. Hemoglobinuria can be

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From the Department of Artificial Organs, The Cleveland Clinic Foundation, and The Frank E. Bunts Educational Institute. Dr. Barlas is now with the Edgewater Hospital, Chicago.

found at the early stage; it disappears within 24 hours when urinary suppression follows. During an operation (when anesthesia masks most symptoms), the most prominent sign may be bleeding from cut surfaces.

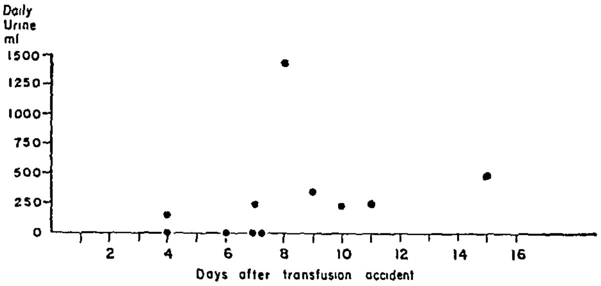

Fig. 1.—Days of oliguria prior to first dialysis and amount of urinary output during 24 hours preceding dialysis.

Oliguric Phase.—The urinary suppression leads to development of uremia. The clinical course greatly depends on the medical management of the patient during this phase. Overhydration leads to peripheral and pulmonary edema and hypertension. Hypertension may lead to convulsions. Even with optimum medical management, accumulation of retention products occurs, leading to mental changes, drowsiness, stupor, psychosis, or coma. Sudden death may occur even in the absence of potassium intoxication. The presence of serious injury, infection, ischemia, or necrosis of muscle precipitates rapid clinical deterioration (and requires early and frequent dialysis).

Diuretic Phase.—The beginning of the diuretic phase is arbitrarily chosen as the time when the urinary output reaches 1,500 ml. in 24 hours. The beginning of diuresis does not end the danger to the patient. Until sufficient tubular function has returned, a high urinary output does not guarantee adequate elimination of nitrogenous waste products or exclude electrolyte imbalance resulting from renal losses. Infections (resistant staphylococcus) and hypertension may still develop.

Acute Phase

Emergency Measures.—On the occurrence of any of the acute signs and symptoms listed above, transfusion should be discontinued immediately. The needle should remain in place for immediate treatment of shock if it develops. Intravenously given fluids, dextran, or compatible blood may be given. Arterenol may be required in addition.

To establish the diagnosis, the physician himself should draw blood from the patient, spin it for hemolysis, and have it cross-matched before his eyes with blood from the incriminated bottle. He should refuse to accept any previously used samples, to exclude the possibility of clerical error.

Specific Treatment.—Intravenous administration of a 5% solution of dextrose in water (2 liters) with 300 mEq. of sodium bicarbonate should be given immediately. This solution is designed to prevent blocking of the renal tubules with acid heme. This measure seems to be beneficial, but only when carried out immediately. It is harmful when renal shutdown has already been established.

Mannitol, 50 or 100 ml. of a 25% solution, may be administered in the hope of increasing urinary flow by osmotic diuresis. This perhaps is useful if given immediately.

Exsanguinotransfusion, according to French authors,[4] should be considered for reduction of free hemoglobin in the blood plasma. Only during the first hours after onset of hemolysis will the free hemoglobin in the plasma be effectively removed.

Oliguric Phase

Maintenance of Body Fluid.—During the oliguric phase insensible loss of water is replaced with at most 500 ml. of fluid per day. Fluid lost by vomiting, diarrhea, abdominal drainage, and whatever small volume of urine is excreted may also be replaced.[5] Even if this fluid restriction is adhered to, gradual overhydration takes place through the catabolism of tissue with release or formation of water. Water in food plus water of oxidation is at least equal to the weight of the diet consumed. Daily body weights are important. As long as the patient is able to take fluids by mouth, he should not be given fluid intravenously except perhaps as

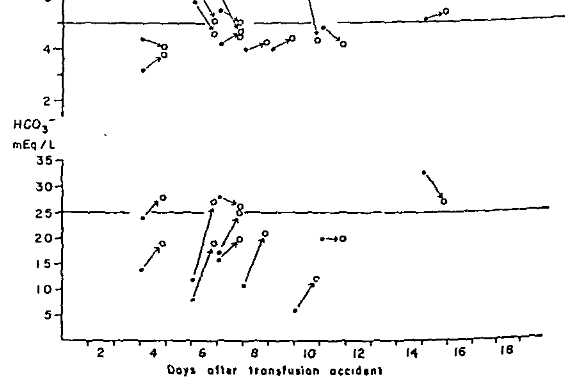

Fig. 2.—*Top,* serum Na^+ and K^+ levels, *bottom,* HCO_3^- level before and after dialysis. Each arrow indicates change of electrolyte level during dialysis.

a vehicle for hypertonic dextrose or fructose. Intravenous infusions in patients with acute anuria carry the risk of acute pulmonary edema or convulsions.

If, during the oliguric phase, overhydration occurs with its dreaded sequelae of cardiac decompensation, hypertension, pulmonary edema, or convulsions, venesection is the most effective immediate remedy for an increased blood volume. During venesection, blood pressure must be measured since the withdrawal of 300 to 500 ml. of blood may be sufficient.

Removal of Edema Fluid.—Sodium sulfate, 45 Gm. in warm water taken by mouth, will retain 1,500 ml. of fluid to make an isotonic solution of 3.2% in the gastrointestinal tract and will cause diarrhea; it is of doubtful value. Peritoneal lavage can remove fluid from the patient if a 3 to 10% dextrose solution is added to the usual composition of the dialyzing fluid. It was not used in this series of patients. The most effective way to remove edema fluid is by ultrafiltration with the artificial kidney. Too rapid loss of large amounts of ultrafiltrate sometimes is followed by mental confusion, but removal of 4 liters per dialysis is possible. The resultant improvement of pulmonary edema is dramatic.

Hyperpotassemia.—Hyperpotassemia is often seen during the oliguric phase. Recognition of hyperpotassemia is best accomplished by determining the serum potassium content with the flame photometer. The electrocardiogram with its very high T waves, broadened QS complexes and low P waves is only a poor substitute for the direct determination. There are several ways of treating hyperpotassemia:[5] 1. Absorption of K+ may be achieved with cation exchange resins (Na+ salt or hydrogen cycle of carboxylic resin or sodium polystyrene sulfonate) in the intestinal tract; 40 to 60 Gm. may be given orally in divided doses or 60 Gm. by repeated high retention enemas.[5] 2. An emergency cocktail may be given intravenously: 10, or 20, or 40% solution of dextrose or invert sugar (40% solution of invert sugar is given into the vena cava), 1 liter; calcium gluconate, 6 to 10 Gm.; sodium lactate, 180 mEq.; and insulin, 20 or 40 units. Thus, effects of K+ on the heart muscle may be postponed until an artificial kidney takes over. 3. Rapid digitalization may be performed. 4. Dialysis with the artificial kidney is the most certain and effective way to reduce any degree of hyperpotassemia within an hour.

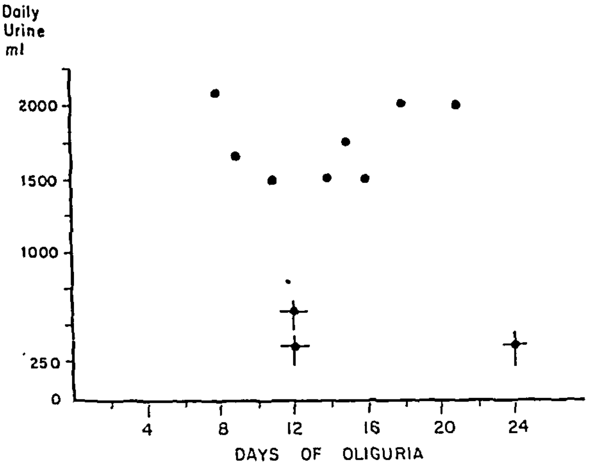

Fig. 3.—Durations of oliguria before beginning of diuresis (urinary output of less than 1,500 ml.): range 8 to 22 days.

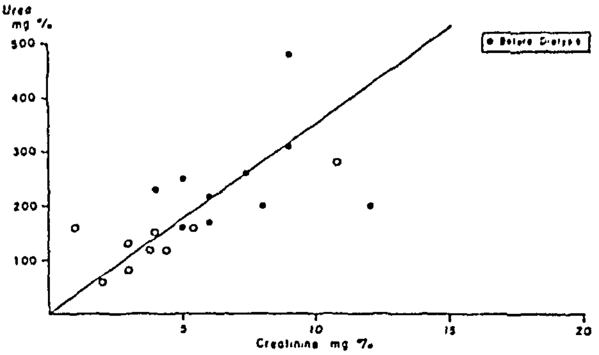

Fig. 4.—Correlation between blood urea and creatinine levels in 11 patients before dialysis (dot indicates values before first dialysis, open circle after dialysis).

Hypocalcemia.—Hypocalcemia is frequent in patients with acute renal failure. It seldom causes symptoms. Convulsions only occasionally are due to hypocalcemia. Tetany usually disappears after intravenous administration of 1 Gm. of calcium gluconate; painful leg cramps sometimes disappear.

Acidosis.—During the oliguric phase acidosis practically always occurs. Carbohydrate is administered to reduce starvation ketosis. If the alkali reserve is lower than 12 mEq. per liter, administration of 40 mEq. of sodium lactate or sodium bicarbonate per day may have to be considered. The sodium salt of carboxylic resin given because of hyperpotassemia is effective in relieving acidosis.

Dialysis provides the most effective means of correcting acidosis. The metabolic acids that have accumulated in the blood are removed and normal constituents, Cl^- and HCO_3^-, are replaced.

Suppression of Protein Catabolism.—We administer a regimen low in protein and as high in calories as is practical for suppression of protein catabolism.[6]

Transfusion.—Only when the hemoglobin concentration is lower than 8 Gm. per 100 ml. should the administration of fresh concentrated red cells be considered. It carries the risk of augmenting the blood volume; with the slightest sign of overloading of the circulation or pulmonary congestion, an equal amount of the patient's blood should be withdrawn. Attempts to raise the hemoglobin concentration to normal will only cause increased blood destruction (1 liter of blood contains 70 Gm. of protein).

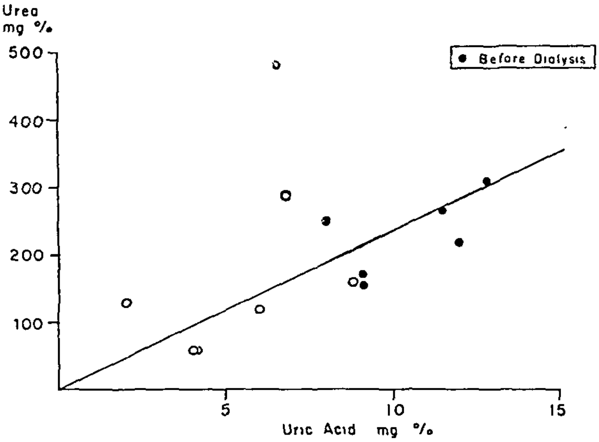

Fig. 5.—Correlation between blood uric acid and urea levels in 11 patients before dialysis.

Prophylaxis and Treatment of Infection with Antibiotics.—Antibiotics often are needed for control of the underlying disease; they should be given prophylactically before pneumonic complications develop in the respiratory tract during a period of stupor or coma. Erythromycin, 2 Gm. on the first day and 1 Gm. daily on the following days, may be administered. Streptomycin, on the other hand, is dangerous because of possible vestibular damage; its administration should not be continued for longer than three days in the presence of anuria.

Artificial Kidneys.—Artificial kidneys were used when the methods described above seemed insufficient to bring about recovery. Disposable twin-coil kidneys were used.[7] Each coil contains two cellulose tubes, 10 meters long. Dialyzing surface for the twin coil is 18,000 sq. cm. The patient is treated with the artificial kidney for a period of six hours. The electrolyte composition of the dialyzing solution resembles that of blood plasma.[8] It takes 1,100 to 1,400 ml. of blood to prime one twin-coil kidney. Dialysis may have to be repeated in three to six days.

Results of Present Study

Between 1954 and 1958, 16 patients having received incompatible blood were seen. The blood was administered for a variety of reasons. Six patients received blood during and after operations, and two received blood because of hemorrhage after delivery. The amount of blood transfused ranged from 1 to 7 pints. A man who received 7 pints of incompatible blood recovered.

The 12 seriously ill patients were treated with dialysis, and 3 of the 12 died. The other four patients recovered without dialysis.

In three patients the transfusion accident happened in large hospitals; two of them did not develop oliguria because the reactions were diagnosed early and the transfusions were discontinued. Thirteen patients were transferred from small hospitals; all were in the oliguric phase.

Three patients had received Rh-incompatible blood: one immediately after delivery and two two and one-half and four years, respectively, after delivery of an erythroblastotic baby. The other patients received simply incompatible blood. For example, a patient with a blood group O received group A. In no case did the trouble result from the use of O donor blood.

Dialysis was performed during the oliguric phase. Only once was it performed in a patient whose urinary output exceeded 500 ml. per 24 hours. Two patients received dialysis as early as the 4th day, and one patient had his first dialysis as late as the 15th day after the accident (fig. 1). The dialyses corrected the serum Na+, K+, and HCO_3^- levels toward normal (fig. 2). In spite of the

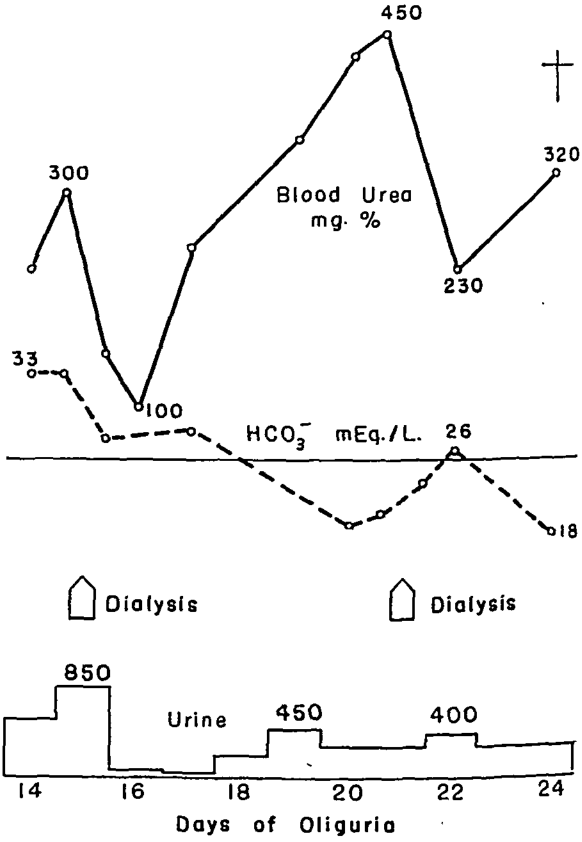

Fig. 6 (case 2).—Predialysis and postdialysis data in critically ill patient with oliguria.

rinsing fluid Na^+ level of 132 to 138 mEq. per liter, the serum Na^+ level after dialysis was often 140 mEq. or more. With one exception, the serum sodium and serum potassium levels were corrected toward normal; the exception was not significant. During dialysis, imbalances of HCO_3^- were corrected toward toward normal. The periods before onset of diuresis ranged from 8 to 22 days (fig. 3).

The elevation of the blood urea level usually parelleled that of uric acid and creatinine levels. In only 2 of 10 patients in whom both were determined was there no parallel between blood urea and blood creatinine levels (fig. 4). On one occasion the blood urea content was high (480 mg.%) with a relatively low blood creatinine content (9 mg.%), which reflects the relatively short duration (six days) of oliguria. In one patient with a blood urea content of only 200 mg.%, the blood creatinine content was high (12 mg.%), in spite of a short duration of oliguria (three days). These findings suggested preexisting renal disease, of which there was no evidence. After dialysis, since both urea and creatinine had been removed according to their gradients, a good correlation between the two was found in all determinations.

There was a good correlation between uric acid and urea levels (fig. 5) in all except one patient. Since dialysis removes retention products according to their gradients, the heights of blood urea, creatinine, and uric acid levels were parallel in all patients after treatment with the artificial kidney.

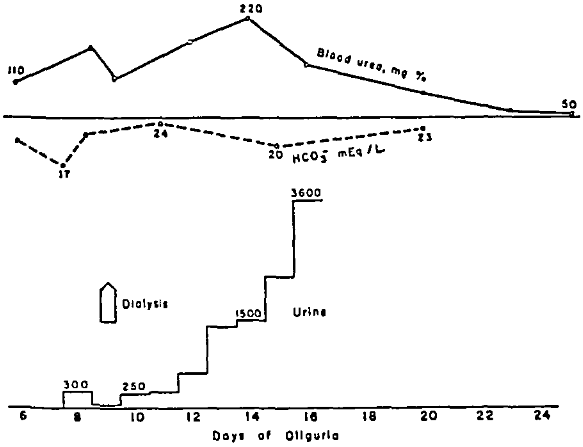

Fig. 7 (case 4).—Data in patient given dialysis.

Report of Cases

Following is a brief review of the cases of 13 patients who developed oliguria after incompatible blood transfusion. At least six patients (cases 1, 4, 5, 8, 9, and 12) would probably not have survived without dialysis. (In the figures accompanying these case reports, the straight line indicates the approximately normal value for blood urea [50 mg.%, high normal], blood creatinine [1 mg.%], serum HCO_3^- [25 mEq. per liter], serum Na^+ [140 mEq. per liter], and serum K^+ [5 mEq. per liter]. Each treatment with the artificial kidney is indicated by a pointed column.)

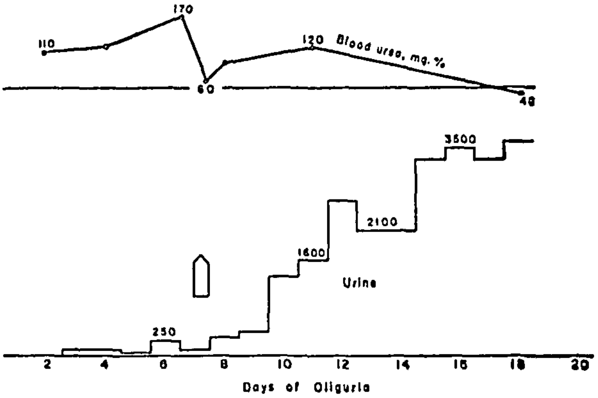

Fig. 8 (case 7).—Data before and after dialysis in patient with low blood urea content and high blood creatinine content.

CASE 1.—A 13-year-old boy was given dialysis at the onset of the diuretic phase because his clinical condition was deteriorating. He recovered.[8]

CASE 2.—A 58-year-old woman was admitted to Cleveland Clinic on the 14th day of oliguria. She had received incompatible blood in transfusion during cholecystectomy and repair of an inguinal hernia. Oliguria, fever, vomiting, and rectal bleeding developed. When she was admitted to our hospital two weeks later, she was unconscious and had general twitching and tremor. She was given dialysis twice. During the second dialysis, complete heart block developed. The blood pressure dropped despite our attempts to maintain it with blood transfusion, mephentermine, and dextran. Her condition deteriorated (fig. 6), and she died on the 24th day of oliguria. Autopsy revealed tubular necrosis and bronchopneumonia; the latter finding explains the continued deterioration.

The fall in blood pressure during the first dialysis may have contributed to the decrease of urinary output after dialysis which far exceeded the usual decrease after dialysis. A fall in blood pressure cannot always be avoided in patients as critically ill as this one was. Every effort should be made to avoid bronchopneumonia.

CASE 3.—A 33-year-old woman had received a blood transfusion during hysterectomy. On the fourth day of oliguria she was given dialysis. She had an uneventful course, with diuresis beginning on the 10th day.

CASE 4.—A 30-year-old woman had a perineal abscess and received incompatible blood in transfusion during an anal fistulectomy. On the next day she passed a small amount of bloody urine. She was admitted here on the sixth day of oliguria. On the ninth day she was given dialysis. Diuresis started on the 15th day. She had an uneventful hospital course after dialysis and was discharged in good condition (fig. 7).

This case illustrates the importance of performing dialysis before the patient's clinical condition deteriorates.

Case 5.—A 40-year-old woman received blood during a major operation and was admitted here on the 10th day of oliguria. She was given dialysis immediately and a second time on the 13th day of oliguria. Diuresis began on the 18th day.[9]

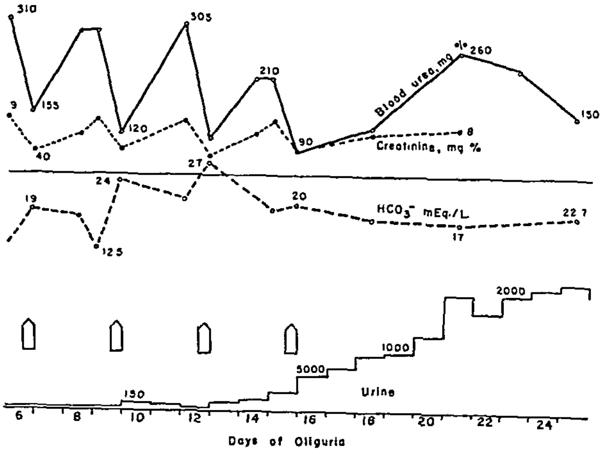

Fig. 9 (case 8).—Results of dialysis in patient who had been given 7 pints of incompatible blood.

Case 6.—A 22-year-old woman recovered from oliguria without dialysis. The potassium level was controlled with resins. Diuresis began on the 13th day.

Case 7.—A 28-year-old woman gave birth two weeks before admission to a baby with Rh-positive blood (the baby had an exchange transfusion). After delivery, because of hemorrhage, she had uterine curettage. She was given a transfusion with Rh-incompatible blood and developed oliguria. On the sixth day of oliguria she was given dialysis. She improved during the next days and was discharged in good condition (fig. 8).

This is an example of a patient with a relatively low blood urea content (125 mg.%) and a relatively high blood creatinine content (15 mg.%).

Case 8.—A 46-year-old man had a nephrectomy. He developed postoperative bleeding, and operation was again performed on the next day, when he received 7 pints of incompatible blood. Severe oliguria and rapid deterioration of his clinical condition developed. He had four treatments with the artificial kidney and recovered (fig. 9). Five months later he was found to be in excellent health.

This was our first experience with a patient who recovered in spite of having been given such a large amount of incompatible blood. We believe that the favorable outcome was due to early dialysis.

Case 9.—A 26-year-old woman was given 2 pints of incompatible blood for metrorrhagia. Acute renal failure with jaundice, nausea, vomiting, and oliguria developed. On the second day of oliguria she was transferred here. Her condition deteriorated, and dialysis was done on the fourth day of oliguria; improvement followed.

A second dialysis was done on the ninth day of oliguria. During her hospital course, potassium-binding resins were given to keep the serum potassium content within limits (fig. 10). She was discharged after a uterine curettage and has completely recovered.

This case is presented as an example of early dialysis indicated by a serious clinical condition that could not be adequately explained by elevation of levels of the usually determined retention products.

Case 10.—A 28-year-old woman developed oliguria after receiving Rh-incompatible blood after a hysterectomy. She was given dialysis on the seventh day of anuria. She recovered.

Case 11.—A 36-year-old woman had given birth to an erythroblastotic baby two and one-half years previously. She received two units of blood after a uterine curettage in a small hospital. Fever, backache, oliguria, and vomiting developed.

On the sixth day of oliguria she was admitted here, acutely ill with a blood urea content of 480 mg. per 100 ml., serum K^+ content of 6.5 mEq. per liter, and serum HCO_3-content of 12 mEq. per liter (fig. 11). She was given dialysis on admission, and her condition improved. Because of rapid, subsequent deterioration she was given dialysis a second time on the 10th day of oliguria. The next day fever developed. A third dialysis was planned for the 15th day. Tracheotomy was done. During the cut-down procedure for the dialysis she died in cardiac arrest due to potassium intoxication. Autopsy showed tubular necrosis.

Case 12.—A 61-year-old woman received a transfusion for anemia. Transfusion reaction was noted and the transfusion was stopped, but it was restarted by another person when symptoms subsided. She was given dialysis twice and recovered.

Case 13.—A 50-year-old woman was admitted to the hospital on the 11th day after hysterectomy and transfusion; she was given dialysis. She died three days later without having improved. Autopsy showed peritonitis and fatty degeneration of the liver.

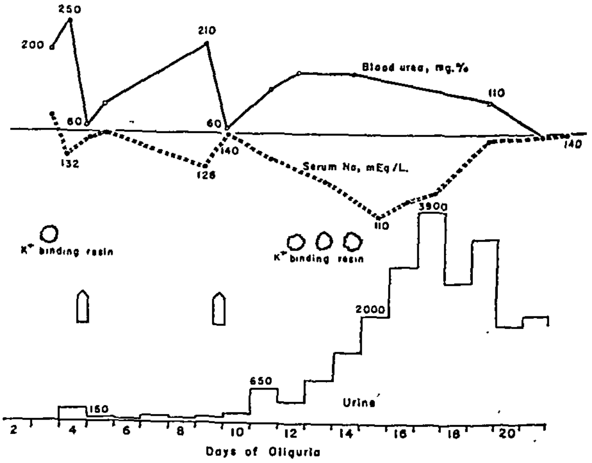

Fig. 10 (case 9).—Results of dialysis in patient with serious clinical condition not explained by elevated levels of retention products.

Comment

Although 13 of our 16 patients were transferred from small hospitals, this means not that transfusion reactions occur less frequently in large hospitals but only that fewer patients were transferred from large hospitals. In the small hospitals the accidents often resulted from mismatching, whereas the three cases in large hospitals resulted from clerical errors. For some patients information concerning the accident was inadequate. Three of the 16 patients died. If two of them had been brought to our hospital earlier, they would have had a chance for recovery or at least for better management. The third patient died from cardiac arrest while preparations for a third dialysis were being made; we failed to anticipate a rapid rise in the serum potassium level. In several of the patients indications for a transfusion were doubtful. The presently prevailing risk of blood transfusion should be more clearly realized.

Indications for treatment of oliguric uremia with the artificial kidney as they developed during the course of this work are as follows: 1. Chemical indications. The blood urea level is higher than 200 mg.%, serum K+ level approaches 7 mEq. per liter, and serum HCO_3^- level is lower than 12 mEq. per liter. The urea content may be out of line with determinations of levels of other retention products, such as creatinine and uric acid. 2. Clinical indications. The patient is stuporous, comatose, or so drowsy that he does not cooperate and does not cough properly. He may be wild, disoriented, or unmanageable. The need for ultrafiltration is indicated by pulmonary edema, hypertension, and convulsions.

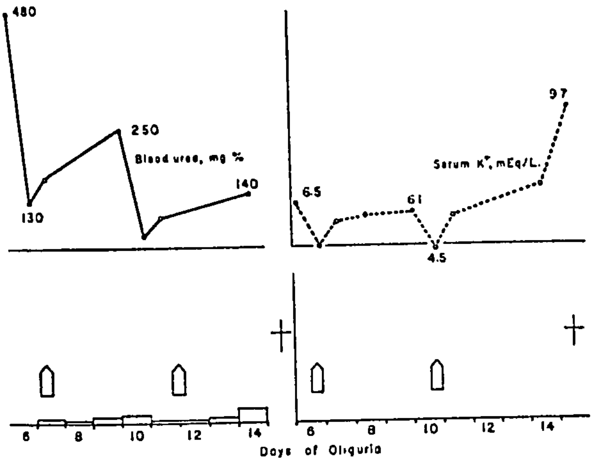

Fig. 11 (case 11).—Cardiac arrest after unanticipated rise in serum potassium level.

An incompatible transfusion is a terrible accident. It becomes a tragedy if the patient is not properly handled. Treatment is best given in a medical center where the staff has experience in the complete management of these cases and where there are facilities for dialysis.

Summary

Between 1954 and 1958, 16 patients in renal failure after transfusions with incompatible blood were treated. Four patients were treated conservatively, and they recovered. Twelve patients were treated with the artificial kidney; nine recovered, and three died. Two of the three patients who died should have been transferred to our center earlier, and one should have received her third dialysis earlier. Disposable twin-coil kidneys were used.

A rise in levels of blood urea and other retention products occurs. In most cases a linear correlation between blood urea, creatinine, and uric acid levels existed, but not always. The medical management of patients with anuria-oliguria includes restriction of fluid intake and prohibition of sodium intake. K+-binding resins lower the serum potassium level, and their sodium salt also tends to correct acidosis. Protein catabolism is discouraged by a high-calorie, low-protein regimen. Prophylactic antibiotic treatment is indicated. Indications for the artificial kidney are chemical (blood urea level greater than 200 mg.%, serum K+ level 7 mEq. per liter, and serum HCO_3^- level lower than 12 mEq. per liter) and clinical (stupor, coma, disorientation, and restlessness). Need for ultrafiltration is indicated by pulmonary edema, hypertension, and convulsions.

2020 E. 93rd St. (6) (Dr. Kolff).

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The twin-coil kidneys used in this study were supplied by Travenol Laboratories, Morton Grove, Ill.

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J.A.M.A., April 25, 1959

TELEVISION IN OTOLARYNGOLOGY AND OTHER SPECIALTIES—A NEW TEACHING DEVICE

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and
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Clinical teaching is difficult when conditions do not permit more than one person at a time to see the part of the body that is being examined or treated. The equipment here described is designed to overcome this difficulty. It is mounted on the instructor's head in such a way as to permit him to observe the interior of an organ directly while a properly aligned and focused television camera picks up an image that can be transmitted to an audience of any desired size. The critical elements of the apparatus are a small, lightweight television camera and a periscopic system with front-surfaced mirror, peep-sight, lens, and prism. The helmet bearing the apparatus is heavy and must be counterpoised. External sources of intense illumination are available. This form of closed-circuit television is useful in clinics, classrooms, operating rooms, and situations arising in postgraduate instruction.

Clinical teaching in otorhinolaryngology has been handicapped by the inability of the examiner to expose the cavities of the ears, nose, and throat for simultaneous inspection by others. The narrow channels of the head that transmit sound outward from the organ of voice and inward to the organs of hearing can be visualized readily only by one person at a time. Similar difficulties beset the gynecologist and proctologist as well as the endoscopist in the fields of urology, otolaryngology, chest surgery, and gastroenterology.

This limitation of observation presents a serious handicap to clinical, classroom, and surgical instruction. Two procedures are currently in general use to alleviate this problem; both have been helpful in selected instances, but neither satisfies the primary need. One of these techniques requires the placement of a small mirror near the viewing axis of the examiner in such a position that the critical image is reflected to a second observer. The second procedure referred to is photography, including both still and motion pictures. The mirror method displays the clinical material immediately, but the observation is sometimes difficult to accomplish and is limited to one additional viewer at a time. Photography, on the other hand, displays the material to many observers but the immediacy of the clinical presentation is lacking.

It is obvious that a procedure which allows an examiner or surgeon to show a specific area deep in a body cavity to any desired number of observers at the moment of examination or treatment provides a greatly improved method of teaching. The accomplishment of this objective depends on the satisfaction of three basic requirements: the examiner must be able to see the field clearly, the equipment must conform to the examiner's movements, and all other observers must be able to visualize the same area as the examiner. It is evident that the third requirement could be met with closed-circuit television, provided the image is received simultaneously by a television camera. This procedure has been demonstrated in general medicine and surgery where standard lighting and camera techniques are applicable. However, when the critical field of observation lies within a restricted channel, the direct view of the television camera is obscured during the process of examination. The fundamental requirement, therefore, for simultaneous viewing and televiewing of the cavities of the head and neck is a positioning of the equipment which allows the camera to receive an image in the optical axis of the examiner. At the same time this arrangement must preserve a direct view of the field and retain freedom of movement for any manipulation. We have developed a practical pilot model of a television-scope that meets these three requirements.

It is evident from the schematic illustration of the equipment (fig. 1) that the mechanism rests on the examiner's head and that the camera gathers its picture by means of a periscopic lens. The light reflected from the subject (fig. 1*A*) travels directly to the eye of the examiner and, at the same time, to the television camera by way of a mirror and lens arrangement (fig. 1*B*, *D*, and *E*). The periscopic system and the camera support provide the necessary mobility for both the examiner and the camera and permit coaxial viewing and televiewing. The details of the components in this combined unit are presented under the three functional divisions which compose it: the optical and television system, the supporting mechanism, and the illumination.

From the Laryngeal Research Laboratory, William and Harriet Gould Foundation, and Northwestern University Medical School.

Optical and Television System

The small, lightweight television camera and the periscopic lens are the critical elements of the present equipment. The optical system is composed of five important elements that will be described in their functional sequence: front-surfaced mirror, peep-sight, lens, prism, and vidicon tube.

Front-Surfaced Mirror.—The front-surfaced mirror (fig. 1*B*) is so constructed and located that it reflects the image upward to the camera lens yet allows the same image to pass through to the eye of the examiner. The cut-away section of the illustration shows the mirror resting in the observer's line of sight at an angle of 45 degrees to the viewing axis. The separation of the image beam may be accomplished by two different types of mirror. In one form the surface is sparsely coated with a reflecting material; in the other the glass is densely covered except for a small clear area in the center. With the partial mirror, the surface is uniform but a reduced amount of light is reflected to the lens, since some light "leaks" through over the entire area. The other, or center-hole, mirror reflects all of the light except at the small central area where the light passes through the clear glass. Both kinds of mirror have been used in this development, but the center aperture type was adopted because it reflects the image with less loss of light and presents a brighter field to the observer. The center opening is not evident in the television image because it is out of the focal range, and the intensity is not noticeably affected as long as relatively large lens apertures are used.

Peep-Sight.—The peep-sight is composed of a pair of holes 3/32 in. in diameter placed 1½ in. apart. These openings are located at the inner and outer ends of the rearward extension of the mirror housing (fig. 1*C*). The size of the holes and their placement enable the examiner to see fields of 1½-in. diameter when the subject-to-mirror distance is 12 in., of approxmately 2 in. at a distance of 15 in., and of 2½ in. at 18 in. These sighted areas coincide with the field covered by the television camera lens and aid the examiner in aiming the camera precisely at the field of interest. This restriction of the field through the peep-sight does not pose any problem for the examiner since his other eye retains full view of the entire field of vision.

Lens.—The lens (fig. 1*D*) used in the present instrument is a modified 6-in. f/4.5 Tessar lens with the elements permanently focused at a subject distance of 20 in. The barrel containing the lens elements is continuous with the mirror housing below and the prism holder above. This unit con-

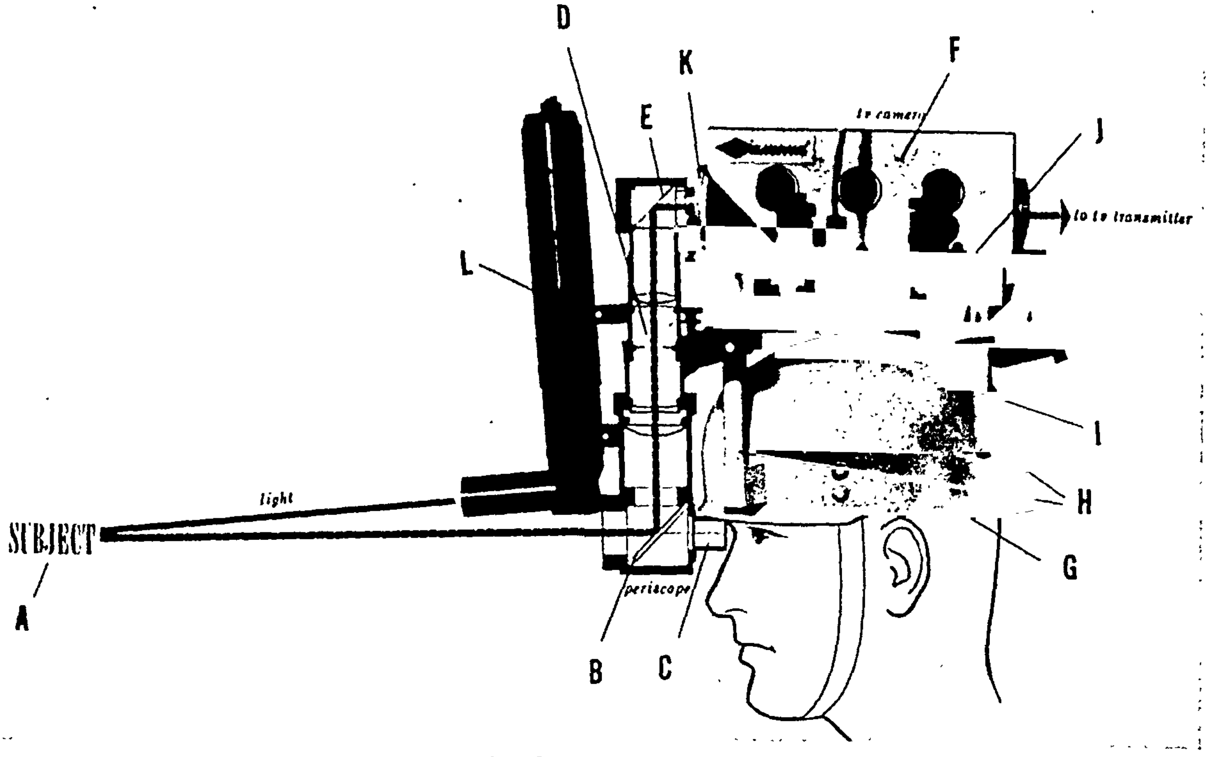


Fig. 1.—Photodiagram of television-scope.

struction maintains a constant eye-level to camera-level distance and adds a desirable rigidity to the assembly. The fixation of the lens elements eliminates the customary type of optical focusing and permits substitution of adjustment at the focal plane, which is described later in the discussion of the vidicon tube.

Prism.—After the image beam traverses the lens elements it is turned 90 degrees toward the television camera by a 1-in. prism that is mounted at the top of the lens section (fig. 1*E*). The housing which supports the prism opens toward the camera and is attached to the supporting structure of the helmet by means of a threaded collar and thumbscrews.

Vidicon Tube.—The final stage in the optical system is the television camera (fig. 1*F*); here the light is focused on the vidicon tube where the visible image is converted to electrical impulses that travel by way of a multiconductor electrical cable to the control equipment and subsequently to one or more television screens.

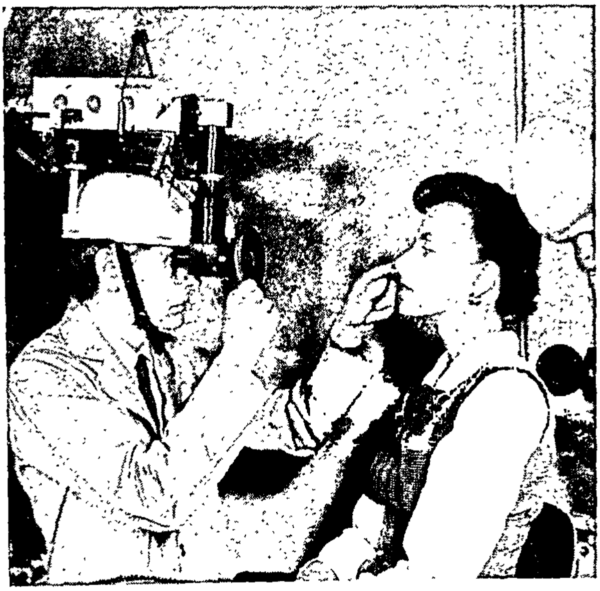


Fig. 2.—Nasal examination demonstrating illumination by means of modified head mirror and detached light source.

There are two systems for obtaining an optical focus of an image on a vidicon tube that may be used with the present equipment: in one type the lens is adjusted while the tube remains stationary; in the other, the lens is fixed and the tube is moved toward or away from the lens. The second method was selected as the more desirable for this pilot model because it is simpler and lends itself to either manual adjustment or remote electrical control.

Supporting Mechanism

The successful application of this periscopic television system to teaching in otorhinolaryngology and other surgical specialties depends to a large extent on the ease and simplicity with which the mechanism can be manipulated. The equipment that supports the operating part must be comfortable, mobile, noninterfering, and adaptable to different persons and situations. The mechanism that supports the television camera and its associated components is composed of two primary parts: the equipment worn on the examiner's head and the counterweighting system that carries the helmet and attached units.

Head Unit.—The basic structure of the unit worn on the head is a Fiberglas helmet (fig. 1*G*) to which four metal tubes 4¼ in. long are attached at equally spaced intervals as indicated by the illustration (fig. 1*H*). At the top of the tubes an aluminum plate (fig. 1*I*), 8⅝ by 10⅛ in., is fastened securely to give rigidity and stability to the foundation structure. The four tubes are fitted with free-sliding rods that are attached at their upper ends to a second aluminum plate (fig. 1*J*) that forms a platform for the television camera. The rods are fastened by pin-and-eye hinge joints that permit the upper platform to be tilted and lifted in relation to the lower plate. These adjustments between the platform and plate compensate for variations in vertical head dimensions among different examiners. The peep-sight must be raised or lowered to accommodate the eye level of the examiner, an adjustment which is accomplished by a corresponding positioning of the camera platform. A simple system of levers connects the two plates at their corners and applies the force that varies the interplate angle and distance; thumb screws lock the levers in their desired positions.

On the upper surface of the platform two auxiliary aluminum plates are mounted for the support and adjustment of the camera. The smaller of the plates, 8⅝ by 5⅛ in., is attached to the underside of the camera and slides toward and away from the lens; this movement accomplishes the focusing mentioned above. The second of the auxiliary plates, 8⅝ by 6⅛ in., holds the sliding camera plate, supports the lens system on the vertical plate (fig. 1*K*), and positions the entire optical-camera system laterally. This side-to-side adjustment combined with the front-to-back and vertical motions described earlier provides a universally adjustable camera support on the examiner's head.

Counterweighting System.—The weight of the equipment attached to the helmet is approximately 18 lb., too much to be carried comfortably without some external assistance. A simple and flexible supporting mechanism was devised consisting of a counterweighted bar resting horizontally on an adjustable vertical shaft. The bar is joined to the upright shaft by means of a ball-bearing bracket that permits the bar to swing around the shaft and provides a fulcrum for vertical movement. A T-shaped unit that suspends the helmet is adjustable along the bar and thereby provides the means of establishing equilibrium. A balanced suspension is the most comfortable and flexible adjustment for the use of this equipment.

Illumination

Two methods of illumination have been used interchangeably with the present pilot model: in one, light from an external source is reflected onto the subject by a modified concave head mirror (fig. 2); in the other method, a beam from a small, high candle power lamp attached to the periscope lens (fig. 1*L*) is directed to the critical area. The reflected light system was developed to simulate the method of illumination used traditionally in the field of otorhinolaryngology. This system offers almost limitless intensity of illumination, since the independent light source can be as powerful as desired. It also provides shadow-free lighting as the result of the beam converging from all points around the lens axis. The principal disadvantage of the reflected light technique is the need for adjustment of the mirror each time either the examiner or the subject moves. When both hands are occupied in an examination or operation, the coincident positioning of the camera and illumination is difficult to manage.

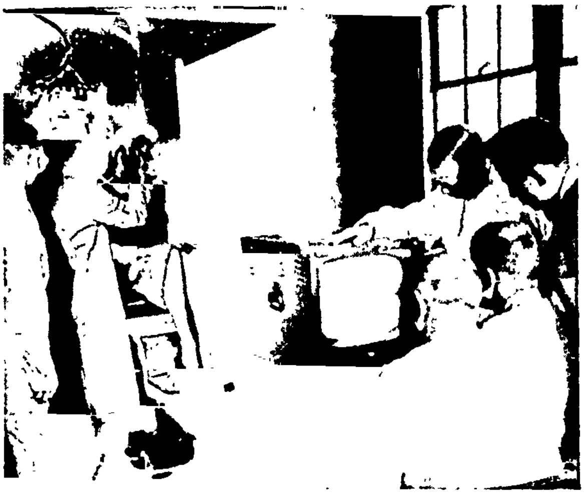


Fig. 3.—Study of tympanic membrane of patient, by means of television monitor, while physician conducts his examination.

This problem of mirror adjustment led to the development of the alternate method of lighting in which a lamp and appropriate lenses are mounted on the optical lens assembly. In this system the camera field and the lighted area are made congruent and secured in this relationship. Consequently, the lens field is always illuminated, which relieves both of the examiner's hands for patient management. The two limitations of the integral lamp in the pilot model are light intensity and parallax factors associated with the positioning of the lamp. Both of these limitations are relatively simple technical problems which are being solved in current development of the equipment.

Applications

We believe there are four teaching situations in which the new type of television equipment, described above, will be particularly useful. The first three, clinic, classroom, and operating room, are illustrated in figures 3, 4, and 5.

Figure 3 shows a group of medical students in an otology clinic studying the tympanic membrane of a patient by means of the television monitor while the otologist conducts his examination. Figure 4 pictures a class of nurses receiving instruction on the functioning of the larynx; and figure 5 demonstrates the equipment in the operating room during operations on the nose and ear. The fourth type of instructional application is an extension of the other three into postgraduate teaching. Closed-circuit television provides the method for disseminating new techniques and information to the physician in his home, office, or hospital. This form of instruction has been used in several branches of medicine, but, with new equipment, this teaching procedure can be extended to otolaryngology and other surgical specialties dealing with deeply placed structures.

Further Developments

The experimental application of the pilot model to various teaching situations has demonstrated that a television camera and associated periscopic lens system supported on the head of an examiner provides a practical means of improving clinical instruction. The developmental program has also revealed several desirable changes in the equipment that should be incorporated in its further refinement. These may be summarized briefly, for the convenience of those contemplating similar developments, into four specific and somewhat interrelated modifications: increase in the depth

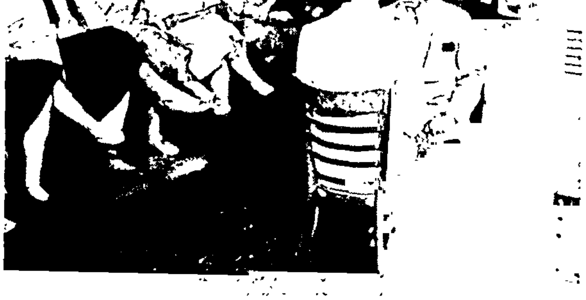


Fig. 4.—Class viewing action of larynx by means of television screens during examination.

of the televised field, variation of field size, modification of the helmet support attachment, and introduction of color television.

Increase of Depth of Field and Variation of Field Size.—In the pilot model the single, fixed, telephoto lens provides maximum magnification of the image at the cost of a shallow field and a relatively small subject area. For teaching purposes it would be ideal if all structures present in the television image could be presented in sharp focus and if the area surveyed by the lens could be made larger and smaller to fit the organ or cavity being examined. Available equipment makes it possible to approach these goals through the selective balancing of such factors as various focal length lenses, size of lens aperture, illumination, and improved television equipment. The pilot model has been redesigned to accept these modifications through provisions for interchangeability of lenses, increased illumination, and a more sensitive television camera tube.

Modification of Helmet Support Attachment.—The suspension of the helmet and associated equipment shown in figure 1 is designed primarily for horizontal viewing. The present range of motion is entirely satisfactory for the usual clinical and classroom demonstrations, but during surgical procedures increased vertical variation is desirable. This maneuverability may be accomplished by attaching the suspension brackets on either side of the helmet at the level of the lower plate, which is close to the axis of vertical rotation and permits easy downward motion of the camera.

Color Television. — The greatest improvement which could be made would be conversion from black and white to color television. The use of color helps to delineate the natural features of the areas being visualized and suggests the three-dimensional character of the field. These features are particularly important in the areas under discussion, where all structures display variations of one and the same color. We hope a small color camera will be developed soon which can be adapted to this televiewing system.

Summary

In the past, clinical teaching in otorhinolaryngology and other surgical specialties has been limited by the difficulty of displaying critical areas within the ear, nose, throat, and other body cavities for student observation. The basic problem has been solved with a small television camera and an associated special periscopic lens system. The device permits direct viewing by an examiner and simultaneous televiewing by others of exactly the same subject area. A complete working pilot model was built and used in several teaching situations in otorhinolaryngology. This application of the instrument demonstrated its practicability and revealed a few desirable modifications that are being instituted in continuing development. With appropriate changes in the optical system, the same principle could be applied to television of similar procedures in various branches of medicine and surgery.

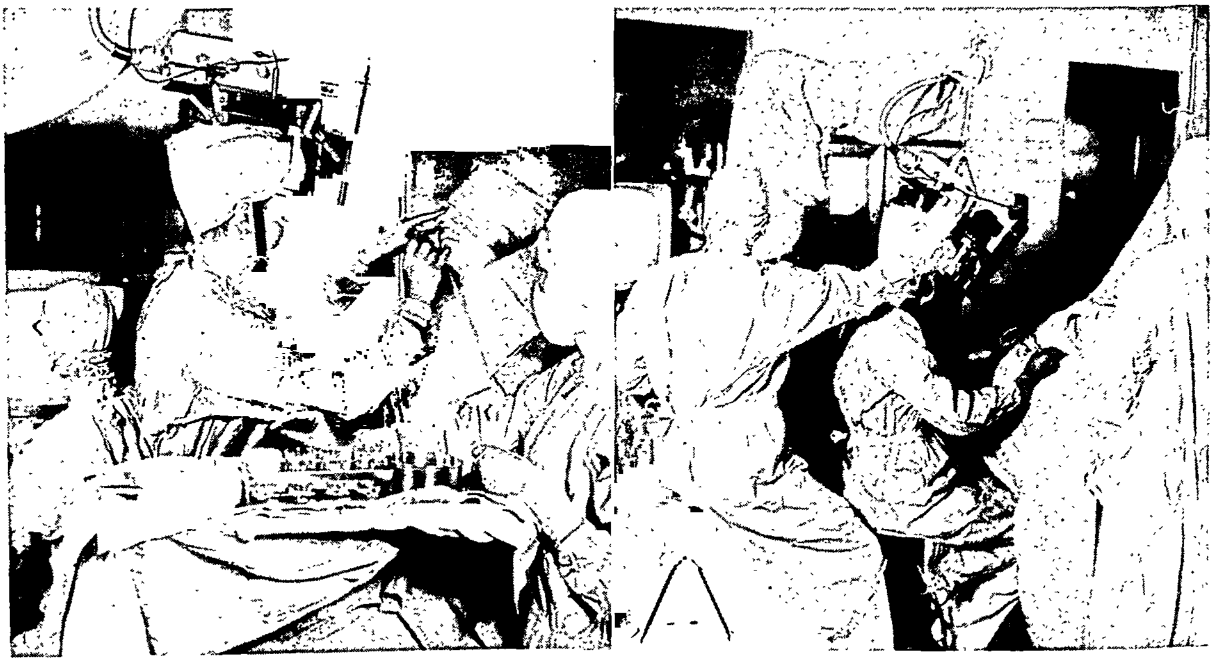


Fig. 5.—*A*, surgeon and television camera simultaneously follow operation in nose. *B*, operation within ear canal is televised for assistants and observers.

159 E. Chicago Ave. (11) (Dr. von Leden).

The television equipment used in this study, Diamond Utilivue Model 500 closed circuit television system, was supplied by Diamond Power Specialty Co., Lancaster, Ohio.

HEART EXAMINATION AND CONSULTATION BY RADIO AND RADIO-PHOTO TRANSMISSION

Arthur Briskier, M.D., New York

The transatlantic sending of heart sounds, roentgenograms, and other essential clinical data is possible. The accuracy of such transmission from New York has been tested by recording the data on tape in Paris and Rome and instantly retransmitting to New York. There was no language barrier when the transmitted records contained no spoken words. The transmitted information, both visible and audible, was received in the form of recordings that could be examined with deliberation and stored for reference. The experiments here reported were concerned with heart conditions, but the possibilities so revealed were far-reaching.

In this age of space travel, when each moment counts, it is important that medical consultations with an appropriate specialist be available at any time and place, particularly in cases of emergency. The best clinical examination, of course, results from personal contact with the patient, and it is the doctor who should make the diagnosis, not the machine. It is not the purpose of the described method to substitute heart auscultation by radio-electronic devices for such examinations, but in emergencies, or when the patient is at a great distance from the specialist, the application of the modern means of communication will undoubtedly prove beneficial.

The radio transmits information of all kinds instantly from one corner of the earth to the other and telephotography similarly transmits photographs. These modern technical facilities are available to medicine. The heart, being the motor of any living body, deserves particular consideration; indeed, my first essays in distance transmissions were records of heart examinations. The first two experiments with transatlantic transmissions of heart auscultation were performed on May 26 and July 3, 1958, from New York to Paris and Rome.

Transmissions

First, the details of auscultation of a normal heart were transmitted through sound tape.[1] In Paris and Rome a recording was made of the transmitted heartbeats. In order to check cardiac acoustic phenomena received abroad, the recorded sounds were instantly retransmitted from Paris and Rome back to New York. It was thus possible to judge the quality of the transmission and the reception through retransmission of the audiovisual records.[2] Within a few seconds the heart sounds crossed the ocean twice, first to Europe and then back to America.

With the heart sounds a visual record was transmitted by radiophotography, containing the clinical data on the patient such as age, sex, height, weight, temperature, and blood pressure as well as a chest roentgenogram, an electrocardiogram, and the symbolic cardio-charting.[3] The transmitted records also contained the results of laboratory tests.

After the successful reception of the audiovisual data on a normal heart, records of certain pathological cases were transmitted, including instances of mitral stenosis, mitral insufficiency, aortic stenosis, and aortic insufficiency. Preoperative and postoperative data on cases of cardiac surgery were then transmitted, including tight mitral stenosis, mitral stenosis with subacute bacterial endocarditis, patent ductus arteriosus with subacute bacterial endocartitis, and tetralogy of Fallot. It would not have been possible to compare at a distance the auscultatory findings preceding and following surgical intervention without the recorded preoperative auscultatory details.

After the surgical records, fetal heartbeats which had been recorded just before delivery were also transmitted along with the normal heartbeats of the mother for purposes of comparison. Audiovisual transmission of cardiac records which are often sufficient can be supplemented if necessary in special cases by direct transoceanic conversations between two medical consultants.

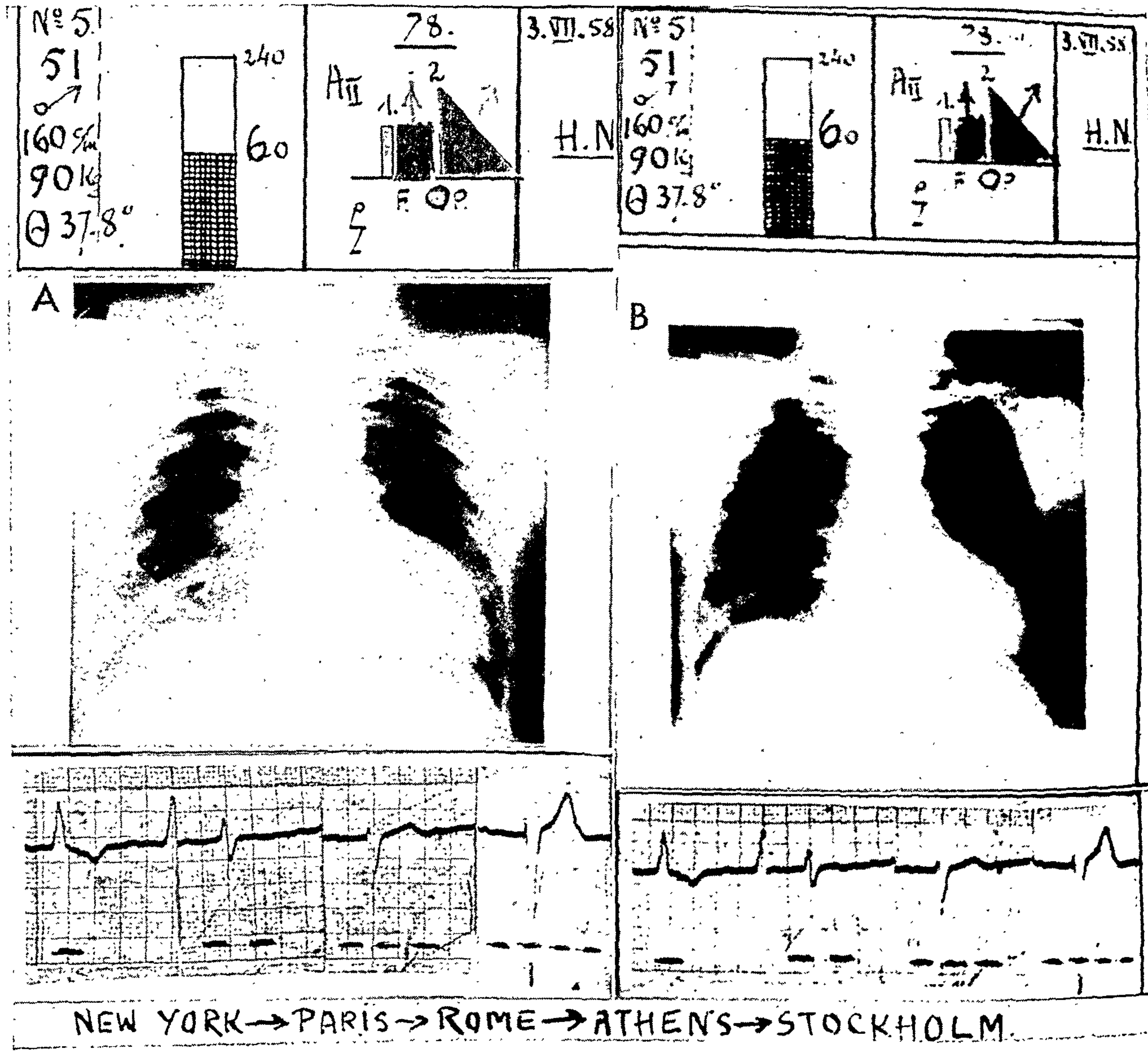
Technique

Cardiac auscultation is first recorded on sound tape[4] through an appropriate microphone and then played back for audible transmission. The recording speed is irrelevant since cardiac frequencies are rather low. While the speed of transmission may or may not correspond to the recording speed, the playback must be at the recording speed. The auscultation can also be directly transmitted, if the cardiac sounds and murmurs are fed directly from the patient's chest through the microphone and the magnetic head to the transmitting instrument.

The visual record, which contains the clinical data, the chest roentgenogram, the electrocardiogram, and the cardio-chart,[5] is located on one side of a sheet of paper which is placed on the drum of the telephoto transmitter. The photograph received in Europe is similar to the original transmitted from New York, and can be used at once for medical interpretation (see figure).

Results.—Abroad, the reactions of the heart specialists to the transmitted records were similar to the reactions these same examiners would have had during an actual examination of the same patients. While the audiovisual record is studied at the point of reception, a copy is transmitted so that patients can be instantly studied, discussed, and compared in the remotest parts of the world by the appropriate specialists while the patients themselves remain undisturbed.

sion of laboratory tests, and communication of therapeutic results; and instant reporting of medical data concerning epidemics and disasters. Although the experiments reported here were concerned exclusively with heart conditions, this method of consultation by radio transmission will prove useful in all fields of medicine, surgery, and obstetrics.



A, visual record transmitted from New York; B, same record a few minutes later at reception in Paris, indicating age, sex, height, weight, temperature, pulse, cardio-chart, chest x-ray, and electrocardiogram. Cardio-chart (top) shows (1) first heart sound; (2) second heart sound masked, following (1) loud rough systolic murmur radiating upward, following (2) soft decrescendo murmur radiating outward and upward best heard at A_{II} aortic region, second interspace.

Applications.—This method has such far-reaching applications as cardiac consultation with specialists located anywhere in the world, particularly when the desired specialist is on a different continent than the patient; in cases of emergency, lifesaving consultations from a plane, a boat, the desert, or the jungle; teaching, demonstration of unusual medicosurgical cases, communication of scientific discoveries; establishment of diagnosis, transmis-

Universality.—The transmitted records contained no spoken words, so there were no language barriers. Because of the simplicity and the clarity of the records, including the self-explanatory symbolic cardio-charting, the messages are instantly understood by all physicians of any nationality.[6] The method is therefore universal in scope and spirit.

Thanks to radio and radiophotographic transmissions of clinical and laboratory data, a new field is open for instantaneous medicosurgical examination and consultation. Thus an interchange of medical and scientific information from and to any distant place is possible. The application of this new method will prove useful therapeutically for both patients and doctors and it should result in a more complete and satisfactory mutual understanding among all doctors and scientists throughout the world.

Summary

Short wave radio and telephoto transmission make it possible to communicate instantly, at any distance, all pertinent clinical and laboratory findings in patients with heart conditions. The first successful transatlantic audiovisual transmissions of cardiac auscultation, including clinical data, roentgenogram, electrocardiogram, and cardiochart from New York to Paris and Rome and back have been accomplished. The audible heart sounds were transmitted by radio through sound tape. The complete visual records were transmitted by radiophotography.

The transmission was successfully received in Paris and Rome, and the sound fidelity as well as the picture quality were crosschecked in New York by immediate retransmission of the records after their reception abroad. This new system can be used in all fields of medicine, surgery, and obstetrics in all parts of the world.

950 Park Ave. (28).

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STAPHYLOCOCCUS AUREUS IN AIR OF AN OPERATING ROOM

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and
Wesley R. Dyer, M.D., Savannah, Ga.

Air-sampling for bacteriological studies was carried out in an operating room for nine days, during which 27 patients were operated on. The 34 colonies of Staphylococcus aureus so obtained were studied as to bacteriophage type. The most frequent type was 80/81. The colonies differed as to sensitiveness to most of the eight antibiotics tested, but all colonies were sensitive to polymyxin B. Eight of the colonies proved sensitive to every one of the antibiotics tested, but there was one colony, not typable, that was resistant to chlortetracycline, chloramphenicol, erythromycin, penicillin, oxytetracycline, and tetracycline. Nontypable colonies were obtained from the nares of two persons working in the operating room. One postoperative infection occurred; the organism concerned was a staphylococcus of type 80/81.

In March, 1958, the U. S. Public Health Service Hospital in Savannah, Ga., created an interdepartmental committee on infections as recommended by the Conference on Staphylococcic Infections in the Hospital and Community.[1] This committee initiated a program to determine the extent of the potential staphylococcic problem within this hospital and requested the assistance of the Technical Development Laboratories of the Communicable Disease Center, also located in Savannah, with the phase of the program concerned with airborne organisms. This paper presents a discussion of some of the findings in air-sampling work conducted to date.

Staphylococcus aureus has been isolated from the air of surgical wards,[2] nurseries,[3] and burn dressing rooms,[4] as well as operating rooms.[5] In spite of this rather common prevalence, the role of air in the transmission of hospital-acquired infections is still

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From the Communicable Disease Center, Bureau of State Services, Public Health Service, U. S. Department of Health, Education, and Welfare, Technical Development Laboratories (Mr. Wolf and Dr. Harris) and the Public Health Service Hospital, Bureau of Medical Services, Public Health Service, U. S. Department of Health, Education, and Welfare (Dr. Dyer).

not clearly defined. Clarke and co-workers,[2] after studying Staph. aureus wound infections in two surgical wards, concluded that spread by contact was the most important route and that efforts to limit spread by contact would be more fruitful than measures directed at airborne bacteria. Nevertheless, Shooter and co-workers [6] reversed the direction of air flow through an operating room so that air entered the theater from out-of-doors instead of from a hospital corridor and thereby reduced the total bacterial counts of the room as well as the number of postoperative infections. One of the latest studies to be reported has been that of Kinmonth and others,[7] in which a curved tube was attached to the inlet of a slit sampler and the open end of the tube was exposed adjacent to the incision of individuals on the operating table. Staph. aureus was recovered on only six occasions, and two Staph. aureus infections occurred when no Staph. aureus was detected in the air. It was concluded that there seems to be little relationship between the development of postoperative sepsis and the presence or absence of Staph. aureus in the theater air. However, the technique of adding a curved tube to the inlet of a sampler, and drawing air through this tube in order to obtain a sample, is a questionable one, since the heavier particles will most likely be trapped in the tube and will not reach the sampler.

Methods of Study

The PHS Hospital in Savannah has a capacity of 150 beds. It was constructed in 1906. The operating theater is on the third floor and comprises a suite of rooms, as shown in figure 1. The rooms are all interconnected and are located adjacent to the main third-floor corridor. Air from outdoors passes through a system of filters and a refrigerated water spray (or through steam-heated coils in cold weather), enters the main operating room under positive pressure through four ceiling diffusers, and leaves through the doorways. An outlet specifically for air is not provided in the main operating room. The air is not recirculated. Temperatures during the sampling days ranged from a low of 64 F to a high of 76 F, and relative humidities ranged from 37 to 78%. The rooms are also warmed by means of steam radiators.

A Casella slit air sampler was used in this survey and was set up in the main operating room near the scrub room door. Settling plates were simultaneously exposed near the slit sampler. The approximate location is shown in figure 1. The site selected for the sampler was based on the desire to obtain as good a sample of air as possible without interfering with the surgical team. It was set up 6 to 8 ft. from the operating table at approximately the same elevation as the table and near an open door through which outgoing air passed.

Two types of mediums were used in the sampling activities, 5% defibrinated sheep blood heart infusion agar and Chapman-Stone (Difco) agar. One or the other medium was used in the slit sampler for an entire day. With the settling plates, both mediums were exposed simultaneously except for one day when blood agar plates only were exposed.

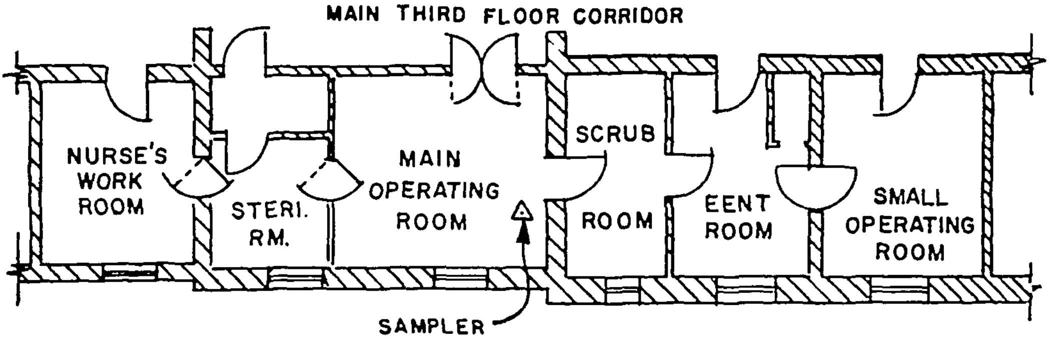

Fig. 1.—Operating suite, PHS Hospital, Savannah, Ga. (scale: 1/16 in. equals 1 ft.).

The slit sampler was operated at a rate of 0.97 cu. ft. per minute. Plates were exposed in this sampler for different intervals of time, varying from 5 to 15 minutes for blood agar plates and 10 to 20 minutes for Chapman-Stone agar plates.

Blood agar plates were incubated at 37 C for 48 hours. Chapman-Stone plates were incubated at 37 C for 24 hours followed by 30 C for 48 hours. All suspicious-looking Staph. aureus colonies on blood agar were streaked on Chapman-Stone agar. Golden-colored colonies on Chapman-Stone agar were transferred to heart infusion agar slants. Gram stains of these transplants were made and coagulase tests performed. In no case was a golden-colored colony on Chapman-Stone agar found which was not coagulase positive. Total colony counts were made on the blood agar plates after 48 hours' incubation at 37 C. A golden-colored colony on Chapman-Stone agar showing gram-positive cocci in typical cluster arrangement and coagulase-positive characteristics was considered as Staph. aureus. The tube coagulase test was employed using desiccated rabbit plasma (Difco). A careful record of the activities in the operating room was maintained while sampling was being done.

Findings

Air-sampling activities were conducted in the main operating room on nine days between March 31 and June 6, 1958. A total of 27 patients were operated on during the sampling days; 3,276.3 cu. ft. of air was sampled in the slit sampler, 1,685.0 on blood agar, and 1,591.3 on Chapman-Stone medium. Blood agar settling plates were exposed a total of 3,748 minutes and Chapman-Stone plates 3,189 minutes.

At least one colony of Staph. aureus (as identified above) was recovered on each of the nine sampling days. The frequency of distribution was as follows: one colony was recovered on each of three days, 2 colonies on each of two days, 3 colonies on one day, 6 colonies on each of two days, and 12 colonies on one day.

Phage Types and Antibiotic Sensitivities of Staphylococcus Aureus Sampled from Air of Operating Room

No. of Colonies	Phage Type*	Antibiotic Sensitivities†							
		Chlortetracycline	Chloramphenicol	Streptomycin	Erythromycin	Penicillin	Polymyxin B	Oxytetracycline	Tetracycline
2	VA4	S	S	R	S	S	S	R	S
9	80/81								
2	80/81	R	S	R	S	S	S	R	R
5	VA4								
1	47								
2	80/81	R	R	R	S	S	S	R	R
1	80/81	S	S	R	S	S	S	S	S
1	VA4	R	S	R	S	S	S	R	S
1	VA4	S	R	R	S	S	S	R	R
1	52A, 80	R	S	S	S	S	S	R	R
1	Not typable	R	R	S	R	R	S	R	R
1	6,77	S	S	S	S	S	S	S	S
1	44A								
1	79								
1	52A								
1	7								
1	29, 52, 52A, 80								
2	Not typable								

* Phage typing by Communicable Disease Center laboratory branch facilities, Chamblee, Ga.
† Intermediate-strength Difco disks. S = sensitive; R = resistant.

Recoveries of Staph. aureus with the slit sampler for the two mediums totaled 18 colonies on blood agar and 12 colonies on Chapman-Stone agar. Correcting for the difference in volume sampled, this represents a yield of Staph. aureus–bearing particles per 100 cu. ft. of 1.07 for blood agar and 0.76 for Chapman-Stone agar, or a ratio of 1.41 to 1. Laboratory tests of the same two mediums, with use of phage types VA4 isolated from an infection and 80/81 isolated from the air, were made in which the two mediums were inoculated with equal volumes of dilute suspensions. The ratios of recoveries on blood agar versus Chapman-Stone agar obtained from these tests were 1.30 to 1 for the VA4 strain and 1.67 to 1 for the 80/81 strain. These ratios show that the recoveries of Staph. aureus from the operating room air with these two mediums are of the same order as would be expected based on laboratory findings.

Only four colonies of Staph. aureus were recovered on Chapman-Stone settling plates. None was recovered on blood agar settling plates. This was probably a chance phenomenon with no relationship to particle size or the kind of medium employed.

All 34 Staph. aureus colonies isolated from the air of the operating room were phage typed. Fourteen were 80/81, nine VA4, and three not typable, while the remaining cultures consisted of one each of the following types: 6,77; 44A; 47; 7; 52A,80; 29,52,52A,80; 52A; and 79. Sensitivities of the Staph. aureus isolated from the air of the operating room were checked against eight antibiotics with use of intermediate-strength Difco disks. The presence of a zone of inhibition without regard to size was interpreted as indicating sensitivity. The order of decreasing effect was as follows: (*a*) polymyxin B, 100% sensitive; (*b*) erythromycin and penicillin, 97% each; (*c*) chloramphenicol (Chloromycetin), 88%; (*d*) chlortetracycline (Aureomycin) and tetracycline, 62% each; (*e*) streptomycin, 29%; and (*f*) oxytetracycline (Terramycin) 27%. The table summarizes the phage types and sensitivities of these colonies.

Two of the operating room staff harbored Staph. aureus in their nares, as determined by single cultures taken by the infections committee. The Staph. aureus in both of these individuals were of a strain that was not phage typable and were resistant to penicillin. During the course of the air-sampling studies, only one colony of Staph. aureus which fits this pattern was isolated from the air. This was obtained 10 days after the cultures were taken from the staff and was the only Staph. aureus recovered on that day. Both individuals were in the operating room at the time this organism was sampled.

The mere recovery of one or two Staph. aureus colonies from the air in a day's sampling time does not provide much of a picture unless the sampling procedure is continued long enough to permit the emergence of some sort of pattern. However, when 6, or better yet, 12, isolates are obtained in a day's sampling, some patterns become apparent.

Data from the three days on which these numbers were recovered from the air of the operating room during the course of this survey are shown in figures 2, 3, and 4. Figure 2 represents the results of May 21, when Chapman-Stone agar was used in the slit sampler. The arrows above the time scale indicate the length of time the slit sampler was operating. Each black dot denotes a Staph. aureus recovery and is *positioned chronologically.* The number above each dot denotes the phage type. The arrows underneath the time scale denote the time interval from the initial incision to the final suture. On this day, all Staph. aureus recoveries were obtained after the lunch hour. In spite of the apparently heavy exposure (5.4 Staph. aureus per 100 cu. ft. of air sampled) of the hernia patient, neither he nor any other patient this day developed a postoperative infection.

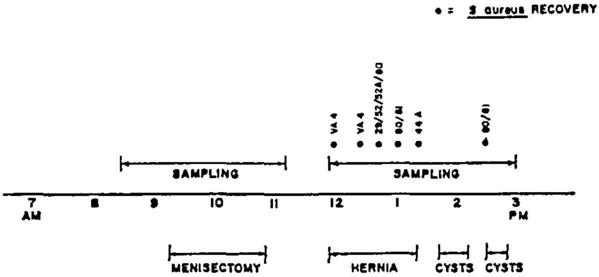

Fig. 2.—Staphylococcus aureus recoveries in main operating room, May 21, 1958.

Figure 3 represents the results of April 21, when blood agar was used in the slit sampler and total counts obtained. Again, the arrows indicate actual intervals of operations, the dots represent Staph. aureus recoveries, and the numbers above denote the phage types. All cultures were phage type VA4. A point of interest on this day was the three colonies that were obtained on the sample which was exposed while the room was swept with a hair broom. The only time a broom was used in the operating room of this hospital was at the end of the day when the amount of debris (mostly sutures) on the floor was too great to be picked up individually by hand. (A mop dampened by a disinfectant solution has now been substituted.)

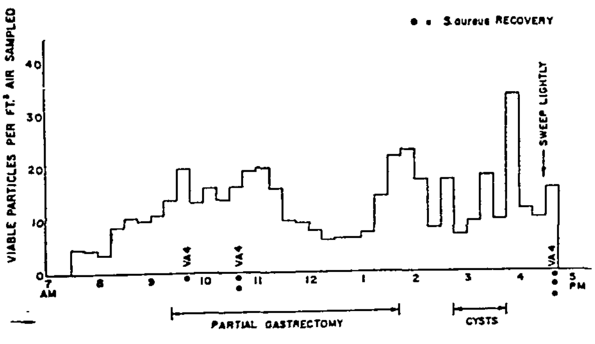

Fig. 3.—Bacterial counts and Staphylococcus aureus recoveries in main operating room, April 21, 1958.

Figure 4 represents the day when the highest recoveries were made (23 Staph. aureus per 100 cu. ft.) and the day a patient became infected. *This patient had a biopsy performed on his right* femur. All four Staph. aureus colonies isolated from the air by the slit sampler while this patient was undergoing surgery as well as the two recovered from the settling plate were phage type 80/81. The subsequent postoperative infection suffered by this patient was due to an 80/81 Staph. aureus.

At the end of this day, the room was swept with a hair broom. Two Staph. aureus colonies were sampled from the air at this time. One was a phage type 7 and the other an 80/81. The sample that followed this was accidentally broken and consequently it is not known how rapidly the Staph. aureus–bearing particles which were apparently stirred up by the sweeping might have settled out. However, none was recovered from the following and last sample of the day, which was taken approximately 10 minutes after sweeping ceased. Duguid and Wallace[8] demonstrated that 90% of the bacteria-carrying particles disappear for various reasons within 35 minutes after an unventilated room is vacated.

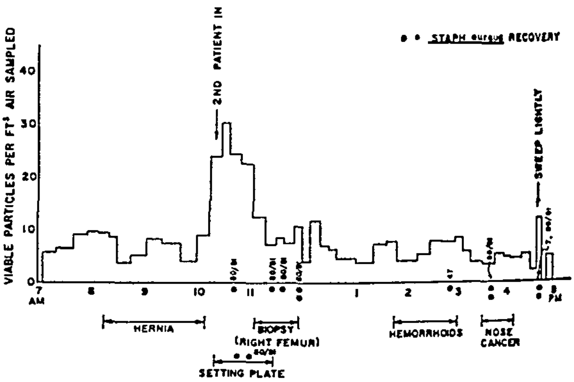

Fig. 4.—Bacterial counts and Staphylococcus aureus recoveries in main operating room, June 6, 1958.

Comment

According to the results with the slit sampler, two individuals were exposed to relatively high concentrations of airborne Staph. aureus. The patient of May 21 did not suffer a subsequent postoperative infection, while the patient of June 6 did. If airborne Staph. aureus was the source of the infection and all the many other variables are equated, what differences can be found in the two cases? First, the May 21 patient was exposed to a peak concentration of 5.4 Staph. aureus–bearing particles per 100 cu. ft., whereas the June 6 patient was exposed to a maximum of 23 per 100 cu. ft. Second, no Staph. aureus colonies were recovered from settling plates on May 21, whereas two were recovered prior to or during the operation of June 6 (a settling rate of 26.5 Staph. aureus–bearing particles per square foot per minute). And third, three different phage types were recovered during the critical interval of May 21, whereas all those recovered during a similar interval of June 6 were of the one type, 80/81.

The data of May 21 and June 6 both indicate a sudden influx of the Staph. aureus into the air of the operating room. (As demonstrated by Shooter and others,[9] Staph. aureus, when present in comparatively large numbers, appears to enter in an explosive manner.) April 21 would have been a "low-yield" day had it not been for the three colonies recovered while the room was swept. The data of May 21 suggest that the operating room personnel and/or the patient brought the organisms in with them after lunch, since no Staph. aureus–bearing particles were obtained prior to lunch and the same personnel were present during the entire day. The data of June 6 show that the patient probably brought the Staph. aureus into the room, since none was recovered prior to his entering and the operating room personnel consisted of the same individuals. This does not eliminate the operating room personnel, since several did leave the operating room for short periods between operations and return.

Conclusions

While we agree that the data of this study are extremely limited, certain findings are worthy of the attention of surgical personnel. 1. A postoperative infection occurred in a patient who was exposed to a relatively high concentration of airborne Staphylococcus aureus of the so-called epidemic strain 80/81. The attending surgical staff were not nasal carriers of this phage type. 2. Sweeping the operating room floor with a hair broom can introduce Staph. aureus into the air. 3. One Staph. aureus–bearing particle was recovered from the air which was similar to the Staph. aureus found in the nares of two individuals among the surgical staff. 4. Staph. aureus, when present in comparatively large numbers, appears to enter in an explosive manner. This entrance might be attributable to the patient or to recent contact of the operating room staff with a source.

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THE GOOD GENERAL PRACTITIONER.—In addition to being the most numerous section of the medical community, the general practitioners are also the most important. . . . He . . . best knows the family history and environment of the patient, and he alone is the arbiter as to where to send the patient in case expert opinion or special treatment is required. . . . The doctor has the highest of all human privileges, to wit, helping others in their troubles, relieving them in their pain, and comforting them in their sorrows. This must, and should, compensate for all the long hours of work, all the heavy responsibilities, and the commonly all too meager financial reward. . . . Now to consider the qualities that should tend to make one a success in general practice. . . . To my mind, the really outstanding qualities are kindness, tenderness and understanding, which enable one to treat the patient rather than the disease. Never forget, no matter how interesting the clinical picture may be, that you are there first and foremost to bring relief to a human being. In nine cases out of ten you will find out that peace of mind is what is being sought rather than ease of body. Especially in the age we live in, when education is more universal . . . and the radio and Press of extreme power, you will tend to find that every pain in the chest is imagined to be heart disease, and every abdominal pain is due to cancer. Fear is the real bogey you will have to fight, and you can't fight fear unless you understand men. Hence, I stress once more that you will be treating human beings more than disease.—D. W. Macnamara, M.B., B.Ch., The Good General Practitioner, *The Journal of the Irish Medical Association,* February, 1959.

J.A.M.A., April 25, 1959

PSEUDO-PSEUDOHYPOPARATHYROIDISM

REPORT OF A CASE WITH ASSOCIATED CARDIOPULMONARY SYNDROME OF OBESITY

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The term pseudo-pseudohypoparathyroidism is applied to a condition in which a patient with dyschondroplasia and ectopic bone formation responds to administration of parathyroid hormone. The patient here described, a 61-year-old woman, had a round facies, short stature, shortened metacarpals and metatarsals, symmetrical deformities of both elbows, and lens opacities. Her response to parathyroid hormone was not studied, but determinations of calcium and phosphorus in her blood suggested normal parathyroid function. Hospitalization was made necessary by excessive drowsiness associated with alveolar hypoventilation and obesity. The patient left the hospital much improved after achieving a weight-reduction of 9 kg. (20 lb.).

In 1942, Albright and others[1] described a familial metabolic disorder characterized by clinical and biochemical signs suggestive of hypoparathyroidism along with a number of physical defects including short stature, broad face, poor mental development, short metatarsals and metacarpals, and ectopic calcification. Intravenous administration of parathyroid hormone (Parathormone) failed to produce the expected phosphate diuresis, and normal or hypertrophied parathyroid glands were noted. This was considered to represent a failure of end-organ response, and the term pseudohypoparathyroidism was coined. In 1952, Albright and others[2] reported the case of a patient with all the physical characteristics of pseudo-hypoparathyroidism but having normal serum calcium and phosphorus levels. The term pseudo-pseudohypoparathyroidism was suggested for this entity and, since the original description, six cases have been reported. The case of pseudo-pseudohypoparathyroidism reported here was complicated by the patient's obesity and alveolar hypoventilation.

Report of a Case

A 61-year-old housewife was admitted to hospital on April 22, 1958, complaining of excessive drowsiness. She had had difficulty with her arms since birth. Her parents and siblings were apparently normal. She had no children.

The patient's face was round and she was short of stature, being 4 ft. 10 in. (147 cm.) tall. Her weight on admission was 228.5 lb. (113.6 kg.) (fig. 1A). Marked mental impairment was noted, and cyanosis, which increased with recumbency or sleep and decreased in the upright position or with hyperventilation. Her right pupil was irregular in shape and there were bilateral lenticular opacities.

The patient was obese, with increased thoracic kyphosis and anteroposterior diameter. There was generalized dulness to percussion over the chest, breath sounds were distant, and there were no adventitious sounds. The apex beat was not palpable. Blood pressure was 140/80 mm. Hg. The abdomen was barrel-shaped and no organs or masses could be felt through the obese abdominal wall.

The patient's legs were short, with pitting edema halfway to the knees. She had difficulty extending both elbows, and movement in the right shoulder was painful and reduced in all directions. Both hands were short and there was displacement of the first, second, and fifth metacarpophalangeal joints on the right hand and the second, fourth, and fifth on the left, with dimpling of the knuckles (fig. 1*B*). No finger clubbing was noted, but the nail beds were deeply cyanotic. Her lower extremities appeared structurally normal.

External genitalia were normal, as was the distribution of hair. No tendon reflexes were elicited and plantar responses were normal. Intertrigo was present in the folds of fat, particularly beneath the breasts.

Laboratory studies yielded the following results: No abnormalities in the urine; hemoglobin level was 16.5 Gm. per 100 ml., erythrocytes 5,500,000 per cubic millimeter; hematocrit value 58%; blood sedimentation rate (Westergren) 7 mm. per hour; and leukocytes, 8,500 per cubic millimeter with a normal differential and platelet count. Serum calcium and phosphate levels, measured on two occasions, were 10.7 and 10.4 mg. per 100 cc., and 4.2 and 5.0 mg. per 100 cc. respectively. Alkaline phosphatase levels, measured on the same occasions, were 10 and 11 King-Armstrong units. The electrocardiogram showed S-T segment depression in 1, 2, aVL, aVF, and from V_2 to V_6. The electroencephalogram was of low amplitude but no abnormality was seen.

Chest roentgenograms showed the heart to be increased in width, with abnormal hilar shadows and pulmonary vascular detail. Skull roentgenograms revealed a small area of calcification or ossification in the falx cerebri. Roentgenograms of the right hand demonstrated shortened first, second, and fifth metacarpals, while the second, fourth, and fifth metacarpals were shortened in the left hand (fig. 2A). The metatarsals of the left great toe were considerably shortened. Roentgenograms of both elbows showed identical deformities (fig. 2*B*), the proximal end of the radius being distorted and articulating with the anterior surface of the humerus close to the capitellum, which was irregular. There was excessive new bone formation around the proximal end of the radius and a suggestion of ectopic ossification around the joint. Roentgenograms of the spine revealed no further abnormalities.

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It was impossible to complete respiratory function studies because of the patient's lack of comprehension and mental dulness. Arterial blood and blood volume studies are shown in the table. It can be seen that there was alveolar hypoventilation with hypoxia, hypercapnia, and moderate polycythemia and that 15 seconds of hyperventilation produced an improvement in the level of blood gases.

Treatment in hospital consisted of an 800-calorie reducing diet, D-amphetamine in daily doses of 10 mg. and analgesics. At discharge from hospital the patient had lost 20 lb. (9.1 kg.) and there was distinct improvement in her color, energy level, and quality of breathing.

Comment

The physical features of a round face, short obese stature, mental dulness, short metatarsals and metacarpals, and normal serum calcium and phosphorus values support the diagnosis of pseudo-pseudohypoparathyroidism. There was no calcification of the basal ganglions, but ectopic ossification was present. The lenticular opacities and the diffuse, low-voltage electroencephalogram are other features previously described. The patient's response to parathyroid hormone was not determined, but the levels of calcium and phosphorus suggest normal parathyroid function. The low-voltage electroencephalogram is of interest but should perhaps not be attributed to this syndrome since hypoxia and hypercapnia may be reflected as nonspecific electroencephalographic changes.[3]

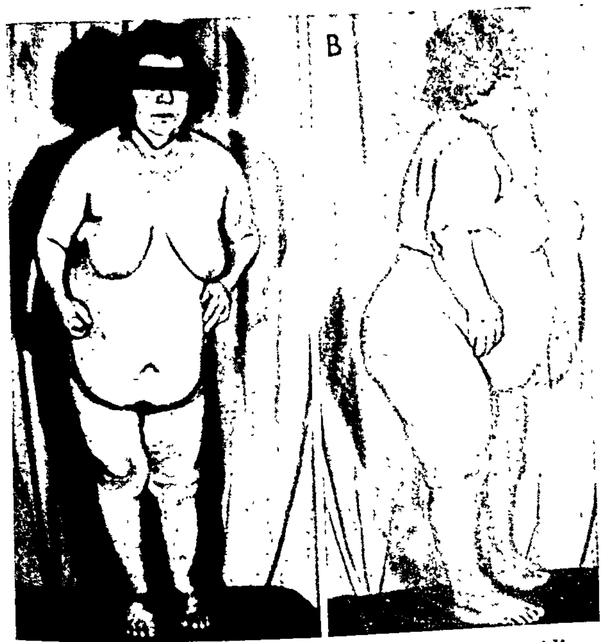

Fig. 1.—Patient with pseudo-pseudohypoparathyroidism; short stature, obesity, deformed arms, and dimpling of knuckles. *A*, anterior view; *B*, lateral view.

The association between obesity and alveolar hypoventilation, secondary polycythemia, and cor pulmonale in the absence of pulmonary disease has recently received considerable attention.[4] The possibility of alveolar hypoventilation with obesity was considered when the patient was noted to be deeply cyanotic and to twitch while asleep. When first admitted she slept almost constantly if not disturbed. She was always startled when aroused, and took several quick breaths which improved her color. The findings of reduced minute volume, hypoxia, and hypercapnia with increased blood volume, increased red blood cell mass, and elevated hematocrit values in the absence of clinical pulmonary disease confirmed the diagnosis of alveolar hypoventilation and secondary polycythemia. These studies were obtained while the patient was awake. Her striking color changes when asleep suggest that the gas tensions would have been markedly abnormal had they been obtained while she was asleep. That these findings were due to the presence of obesity can only be postulated since it was not possible to repeat the studies after

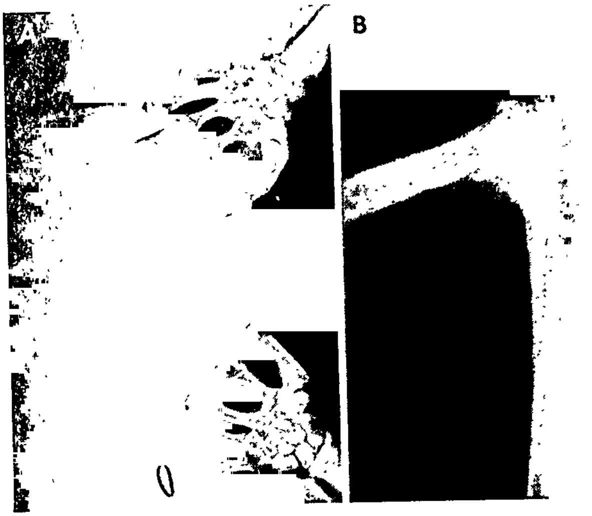

Fig. 2.—*A*, roentgenogram of both hands; shortened first, second, and fifth metacarpals of right hand and second, fourth, and fifth metacarpals of left. *B*, roentgenogram of elbow; irregularity and displacement of elbow joint with excessive bone formation around proximal end of radius.

Pulmonary Function and Blood Volume Studies

Study	Patient	Normal
Ventilation,* liter/min.	6.8	6-10
Respiratory rate	20	
Tidal volume, cc.	340	500-800
Dead space, cc.	160	120-180
Dead space/tidal volume ratio, %	47	<30
Arterial, at rest		
pO_2, mm. Hg	66(88)†	>90
pCO_2, mm. Hg	46(42)†	35-44
pH	7.40	7.35-7.45
hematocrit value, %	58	
Blood volume (ml./sq. m.)		
total	2,900	2,250
plasma	1,216	1,270
red blood cells	1,682	986

* Body temperature, ambient pressure, saturated with water.
† Value in parentheses obtained during hyperventilation.

the patient's 20-lb. weight loss, but the clinical improvement indicates the possible association, in her case, of excessive weight and altered arterial blood gases. In addition, the marked improvement in arterial oxygen tension after slight hyperventilation further suggests that the lungs were normal. It is of interest that it was the symptoms resulting from alveolar hypoventilation which led to the hospital admission of this patient.

In addition to the original case six patients with pseudo-pseudohypoparathyroidism have been reported in the world literature. In 1955, Miles and Elrick[5] described a 25-year-old woman with the typical physical features including lenticular opacities but without ectopic calcification. Roche and others[6] described a 40-year-old man with dyschondroplasia and ectopic calcification but normal configuration and facial contour. In addition, he was noted to have blue scleras. Wallach and others[7] in October, 1956, described a 24-year-old man with striking subcutaneous ossification but neither short metacarpal and metatarsal bones nor short stature and round face. The dyschondroplasia was restricted to short distal phalanges. He also had gout, unexplained splenomegaly, lymphoid hyperplasia, and asymptomatic rheumatoid spondylitis. McNeely[8] and others described a 24-year-old man manifesting brachydactylia and short stature with soft tissue calcification and ossification. Seringe and Tomkiewicz[9] recently reported two sisters, aged 15½ and 10½, who were short, bordering on dwarfism, with short necks, slightly rounded facies, and pronounced brachymetapody. In both patients and in the otherwise normal mother blue scleras were noted. In 1956, Cusmano and others,[10] in a report of six cases of pseudo-hypoparathyroidism, mention that the mother of one of the patients in the series showed short stature, short metacarpals and metatarsals, and undoubtedly represented a further case of pseudo-pseudohypoparathyroidism.

Albright's concept of the syndrome of pseudohypoparathyroidism was that it consists "of several unrelated genetic defects which occur simultaneously," including unresponsiveness to parathyroid hormone, dyschondroplasia, and ectopic bone formation. The term pseudo-pseudohypoparathyroidism was applied by Albright to individuals with the second and third defects but without the first; thus, the initial report on pseudo-pseudohypoparathyroidism tended to confirm the view that dyschondroplasia and ectopic bone formation were genetically separate from the failure of responsiveness to parathyroid hormone. The term pseudo-pseudohypoparathyroidism is perhaps an unfortunate one since it has suggested to some that it is a forme fruste of pseudo-hypoparathyroidism. Discovery and definition of the metabolic errors distinguishing these defects will undoubtedly provide a more useful term.

Summary

A 61-year-old woman with round facies, short stature, shortened metacarpals and metatarsals, lens opacities, and normal parathyroid function fulfilled the criteria for a diagnosis of pseudo-pseudohypoparathyroidism. Her excess weight and abnormal respiratory function satisfied the necessary requirements for the diagnosis of alveolar hypoventilation associated with obesity. Excessive drowsiness associated with the alveolar hypoventilation probably precipitated the hospital admission.

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TREATMENT OF ACUTE TYPHOID WITH SYNNEMATIN B

REPORT OF A CASE

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The use of synnematin B in the treatment of typhoid in infants and children in the Hospital Infantil, Mexico City, was reported in 1955 by Benavides and associates.[1] Synnematin B was shown to be effective in the treatment of acute typhoid as indicated by the fact that no deaths or perforations were observed in this series of cases. It is of interest to note that Salmonella typhi was cleared from both blood and feces of all patients and that no indications of toxicity referrable to the drug were reported. Of further significance is the fact that the development of the carrier state has not been observed in any patient adequately treated with synnematin B.

The present report is believed to be the first paper published on the clinical use of synnematin B in typhoid in the United States. It is an account of acute typhoid in an adult which responded dramatically to treatment with synnematin B after failure of chloramphenicol (Chloromycetin) to effect a favorable clinical response.

A patient with a severe systemic infection was treated unsuccessfully with penicillin, chloramphenicol, and a third unidentified antibiotic. Salmonella typhi was cultured from blood and feces and was found sensitive to synnematin B. The condition of the patient had become very critical when therapy with synnematin B was begun, and it continued to be critical during the first 48 hours. Thereafter, improvement was rapid. Eleven days after discharge the patient was readmitted with typhoid peritonitis ascribed to rupture of an infected ovarian cyst. From this setback the patient recovered without any antibiotic treatment, and subsequent tests indicate that she is not a carrier. Her son and father-in-law also had mild forms of typhoid; they recovered on treatment with chloramphenicol.

The patient's family, consisting of husband, wife, and son, entered Mexico for a vacation on Feb. 6, 1956. On Feb. 16, the wife developed mild diarrhea which persisted until Feb. 20. The family returned to Michigan on Feb. 25. On Feb. 27 the patient noted a return of malaise and diarrhea and had a chill, and on Feb. 29 she developed fever, headache, cough, and occasional chill. Treatment for three days with penicillin and an unidentified wide-spectrum antibiotic ordered by a local physician was ineffective. From March 3 to March 9 she had no treatment and became progressively worse. On March 9, one of us (F. C. G.) made a clinical diagnosis of typhoid and started oral treatment with chloramphenicol (250 mg. every six hours). The patient's condition deteriorated, and she was admitted to the hospital on March 10, 1956. A summary of this case is presented in the figure.

Therapy with intramuscularly given chloramphenicol was also instituted on admission. S. typhi was isolated from both blood and feces on March 11 and 12. Results of the Widal agglutination test done on March 11 were reported as follows: S. typhi O antigen 1:10,240, H antigen 1:80, and S. paratyphi B 1:160. The patient's condition continued to deteriorate while she was on chloramphenicol therapy. On March 13, 1956, she was semicomatose and bleeding grossly from the intestine, had a spiking temperature with peaks at 104.4 F (40.2 C, oral temperature), and was considered to be in a critical condition.

Physical examination on March 12, 1956, prior to starting synnematin B therapy, revealed an acutely ill, well-nourished woman, 37 years of age, weighing 212 lb. (96.1 kg.). She was semicomatose, had a nonproductive cough, and apparently had some difficulty in hearing. Oral temperature was 104.4 F, the pulse regular at 100 per minute, blood pressure 130/84 mm. Hg, and respiration rate 32 per minute. The positive findings may be summarized as follows: typical rose spots on the abdomen, otitis media with hearing loss on the right side, acute bronchitis, and abdominal distention with tenderness which was interpreted as indicating impending perforation of the intestine. On March 12, the blood analysis was reported as follows: hemoglobin level 12.8 Gm.%, 4,010,000 red blood cells per cubic millimeter, and 4,100 white blood cells per cubic millimeter (42% segmented neutrophils, 23% nonsegmented neutrophils, and 35% lymphocytes). Urinalysis on March 12 revealed a specific gravity of 1.005, 3+ albuminuria, and 4-10 white blood cells and 3-6 red blood cells per high-power field. In view of these physical and laboratory findings, the diagnosis of typhoid was confirmed.

The cultures of S. typhi isolated from the blood and stool on March 11 were sensitive to less than 1 unit per milliliter of synnematin B. Chloramphenicol therapy was stopped after the morning dose on March 13. Therapy with synnematin B was started at 7:30 p. m. of that day with a dosage schedule of 80,000 units per kilogram of body weight per day in divided doses, intramuscularly, every four hours. In addition to synnematin B, this patient received supportive care and aspirin for temperature control. No other antimicrobial substances were used after synnematin B therapy was started.

During the first 48 hours of synnematin B therapy, the patient continued to be in a very critical condition. Rectal bleeding continued for about 24 hours but was not observed again after the first full 24-hour period of this therapy. After 48 hours of synnematin B therapy there was a dramatic change in the patient's condition. On the morning of March 16, she felt considerably improved and evidenced interest in food for the first time since being admitted to the hospital. The hearing loss on the right side disappeared, as did her cough. She was well oriented as to time and place. From this

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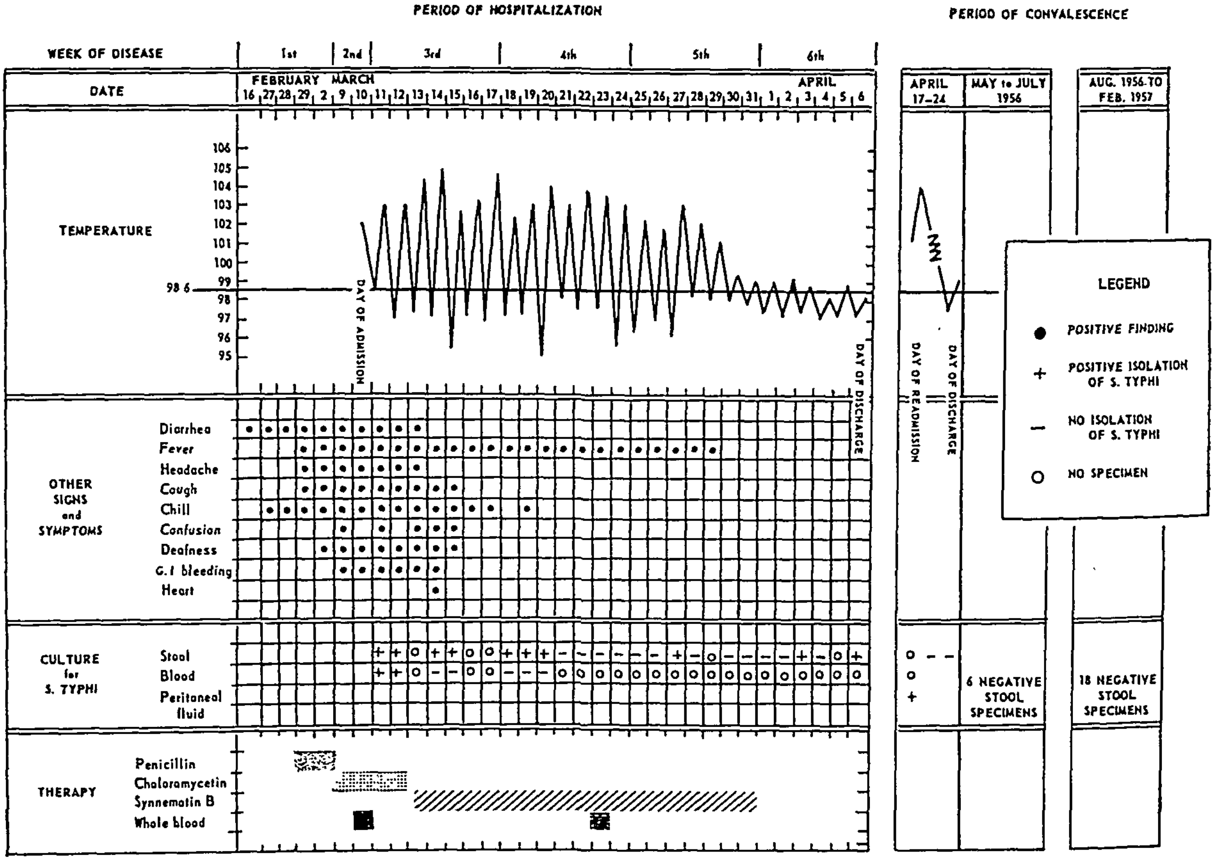
point on, she continued to make steady improvement with no indication of relapse being observed. However, her clinical course was not without incident.

On the second day of therapy, the patient developed a transitory gallop type of cardiac rhythm, followed by auricular fibrillation which was accompanied by an apical systolic cardiac murmur. In view of the tachycardia which was also present, it was felt that a complication was imminent. The abdomen was tender but not distended, and intestinal sounds were present. Perforation did not occur. The incident passed and the cardiac arrhythmia did not recur.

After the patient received 10 grains (0.65 Gm.) of aspirin when her temperature was 104.8 F (40.4 C) at 12:30 p. m. on March 14, the temperature fell progressively and by 7:30 p. m. a temperature of 95.4 F (35.2 C) was recorded. Subsequently, the dose of aspirin was limited to 5 grains (0.32 Gm.). (Osler and McRae [2] have cautioned against too vigorous use of antipyretics in typhoid.) Fever persisted throughout the course of therapy, resolving gradually by lysis; this situation has also been observed by Benavides and associates.[1] The drug therapy was stopped on March 31. The patient's condition continued to improve, and she was discharged from the hospital on April 6, 1956.

On April 17, 1956, she was readmitted to the hospital because of abdominal pain and distention. Laparotomy revealed a ruptured ovarian cyst, subsiding inflammation of the appendix, and peritonitis. A pure culture of S. typhi was isolated from the peritoneal contents. No evidence of perforation of the intestines was observed. This incident presented several unusual aspects, which will be discussed in a separate report.[3]

Because the findings at operation did not reveal intestinal perforation and there was nothing to suggest a relapse, it was decided not to give a second course of synnematin B therapy.



Graphic summary of case of typhoid treated with synnematin B.

The abdomen was closed with drainage, and the patient made an uneventful recovery. She was discharged from the hospital on April 24, 1956.

As required by the Michigan Regulations for the Control of Communicable Diseases,[4] follow-up studies were done for three months by the attending physician (F. C. G.) and the Eaton County (Michigan) Health Department with examinations of stool specimens for S. typhi. In addition, follow-up examinations were given for a period of one year with monthly examinations of stool specimens and for another year with examination of occasional stool specimens. The last positive isolation of S. typhi from the intestinal tract of this patient was on April 6, 1956. It is therefore assumed that she is not a carrier of S. typhi.

While this patient was in the hospital with typhoid, her 12-year-old son also was hospitalized and subsequently shown to have a mild case of typhoid. He was placed on chloramphenicol therapy and made an uneventful recovery, being discharged on March 24, 1956. He was also given follow-up examinations, and stool specimens were examined by the Eaton County Health Department. S. typhi was isolated from his specimens on April 30 and May 26, 1956. All stool specimens submitted since May 26, 1956, have been negative. According to the definitions set forth in the regulations, this boy would be classified as a convalescent typhoid carrier.

The father-in-law of the patient was in close contact with her during the early phase of her illness. He developed a mild case of typhoid, but he refused hospitalization and was treated at home with chloramphenicol. Stool specimens submitted by him on March 28 and 29 and on April 5, 1956, were positive for S. typhi. All subsequent specimens have been negative. This man would also be classified as a convalescent typhoid carrier. The husband of the patient did not develop any evidence of infection with S. typhi.

Comment

The response of a patient with typhoid to treatment can be judged from several points of view, including the well-being of the patient, clearance of S. typhi from the blood stream and intestinal tract, response of the fever, presence or absence of complications, duration of illness, presence or absence of toxicity, development of the carrier state, and death rate. Several of these points are applicable to the judgment of effectiveness of synnematin B in the treatment of the case of typhoid presented in this report.

As reported by Benavides and associates,[1] a definite improvement was noted in the general well-being of the patient after the first 48 hours of synnematin B therapy. At this point in the course of the disease, there was a renewed interest in food and increase in appetite, a decrease in toxic manifestation, and an improvement in mental alertness which also characterized this case. At the time synnematin B therapy was instituted, chloramphenicol had been used for four days and there was imminent danger of intestinal perforation. Smadel and co-workers[5] have emphasized the fact that serious complications, such as intestinal hemorrhage and perforation, may be expected to occur in patients treated with chloramphenicol, since the stage is generally set for such developments before therapy is instituted and time is usually required for the healing of the typhoidal lesion of the intestine. However, rectal bleeding stopped after our patient received synnematin B therapy for 24 hours and was not observed again. Inflammation of the ears and respiratory system, as represented by otitis media and bronchitis, resolved promptly without the development of mastoiditis or pneumonia. S. typhi was cleared from the blood within 24 hours after starting synnematin B therapy.

The typhoid organism was not cleared from the stool until 25 days after treatment with synnematin B was started. S. typhi was isolated from the stool specimen collected six days after antibiotic therapy was concluded. However, the organism was not isolated from the stool of this patient on any subsequent occasion. In other words, the carrier state did not develop in this patient. This result may be constrasted with that of the son, who was treated with chloramphenicol and continued to excrete S. typhi for at least two months after treatment. The fact that infants and children treated adequately with synnematin B do not develop into chronic carriers was reported in the series treated by Benavides and associates.[1] This report may be contrasted with the recent publication of O'Connor,[6] who stated that 1% of patients treated with chloramphenicol became carriers, as contrasted with 2% of the control group who received nonspecific therapy. This difference in carrier rate among the treated and control groups was not considered to be statistically significant.

It is well known that the carrier state develops most commonly in adults and that chronic carriers of S. typhi are more common among adult females than among adult males or children. Evidence summarizing the use of synnematin B in infants and children and in the one adult reported here indicates that the chronic carrier state does not develop among adequately treated patients. However, the influence of synnematin B on the development of the carrier state in adults awaits further evaluation.

During the first two days of synnematin B therapy, the patient continued to be critically ill with a rising temperature. Previous work[7] with synnematin B has shown that the drug is bactericidal in its action. It is our belief that this bactericidal action, combined with the defense mechanisms of the host, resulted in the release of a considerable quantity of typhoid endotoxin into the circulation. This substance, known to be pyrogenic, is thought to be responsible for the continued fever and chills observed in this patient during the course of therapy with synnematin B.

The possibility must also be considered that synnematin B is pyrogenic and that the drug was responsible in part for the high temperature. The fever curve indicates that the temperature was returning toward normal by lysis during the last seven days of therapy. Also, the injections were continued for 30 hours after the patient became afebrile. Our own studies[8] in human volunteers, patients with urinary tract infections, and animals have not revealed any pyrogenic tendency on the part of synnematin B. Therefore, we have concluded that synnematin B is not pyrogenic. No evidence of toxicity which could be attributed to synnematin B was observed in our patient. A similar observation was made by Benavides and assocates.[1]

The isolation of S. typhi from the peritoneal contents at the time of the second admission raises the questions of perforation and relapse. There was no evidence to support a diagnosis of relapse. Therefore, the patient was not treated further with synnematin B.

Since bacteriological examination of the liquid contents of the peritoneal cavity revealed a pure culture of S. typhi, in all probability it did not arise from a perforation of the intestines. When intestinal perforation does occur, the peritoneal contents usually yield a mixed culture, representative of the contents of the intestines at the time of perforation.

The biopsy of the cyst during laparotomy revealed the typical structure of an endometrial cyst of the ovary. If this cyst contained S. typhi after the septicemia of the acute illness, a rupture of the cyst would produce a pure culture typhoid peritonitis. Therefore, the most probable explanation would be that the S. typhi was walled off in the cyst during the acute phase of the disease. This conclusion would agree with the coincidence between the ruptured ovarian cyst and the peritonitis without perforation, as well as the pure culture of S. typhi reported by the bacteriologist. A more detailed discussion of this incident will be reported in a separate paper.[3]

Summary

A patient with acute typhoid was treated, with good response, with synnematin B. No perforation occurred, the patient rapidly regained a feeling of well-being, and there was no evidence of toxicity after the use of synnematin B. The patient developed peritonitis associated with a ruptured endometrial cyst of the ovary early in the convalescent period. The carrier state did not develop, as evidenced by follow-up studies extending over a period of two years.

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J. M. Cook, M.D., director, and the staff of the Eaton County (Michigan) Health Department assisted in completing surveillance during convalescent period.

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FAVORABLE RESPONSE IN THE CLINICAL TREATMENT OF CHRONIC ALCOHOLISM

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The community clinic approach for the rehabilitation of chronic alcoholics is being used with increasing frequency in the United States. In line with this trend, Maryland has established six county alcoholic rehabilitation clinics through the collaboration of state and local health departments. These were set up as part-time evening clinics and staffed with personnel representing the traditional psychiatric team plus a public health nurse. Treatment methods consisted of individual and group treatment of the alcoholic and occasionally of the spouse. In order to develop, extend, and improve the program, it was felt necessary to appraise the effectiveness of the services offered. A survey was initiated to meet this need. One of the major goals was the identification of some of the factors which contribute to a favorable outcome in the clinical treatment of alcoholism. In this paper only data relevant to these favorable factors are described.

The records of 57 men and 20 women patients in six county rehabilitation clinics for alcoholics were studied in order to identify the factors favoring recovery. Treatment included both individual and group psychotherapy. Criteria of improvement included the amount or frequency of alcohol-consumption, family and social adjustment, occupational adjustment, and physical appearance, and 42% of the patients improved on three or more of these criteria. The greatest improvement was found in those who attended the most treatment-sessions, whose spouses participated in the sessions, and whose relatives received routine social service contacts. The people attracted to these clinics were of a socially stable type in extreme contrast to the alcoholic stereotype. The unusually favorable results obtained demonstrate the importance of considering groups, especially the family, in future planning for the outpatient treatment of chronic alcoholism.

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†Dr. Gliedman died May 20, 1958.

A multidisciplinary research team developed special rating scales, information schedules, and interviews to evaluate the treatment results of the six clinics. These scales were given to the therapists who completed them retrospectively for each of the patients in treatment during the three-month survey period. The sample of 77 patients and 12 spouses was studied from the standpoint of selected personality attributes, amount and type of therapy, attendance at clinics, and therapeutic changes as measured by multiple criteria.

TABLE 1.—*Percentage Change in Clinical Population of Seventy-seven Patients on Four Criteria of Improvement as Compared to Initial Status*

Rating	Drinking (Amount or Frequency)	Family and Social Adjustment	Occupational Adjustment		Physical Status*
			Employed	Unemployed	
Abstinent	35				
Much less	17				
Somewhat less	17				
Unchanged	26				
Somewhat more	3				
Much more	...				
Out of control	3				
Better		51	40	45†	39
About the same		42	53	45	59
Worse		7	8	10	3

* Rating based on appearance only.
† Now employed.

These criteria included (1) drinking (amount and/or frequency) as compared to initial status, rated on a seven-point scale from "abstinent" to "out of control," (2) family and social adjustment, (3) occupational adjustment (depending on whether or not the patient was employed at the start of treatment), and (4) physical status as compared to initial impression of physical condition, all compared to initial status and rated on a three-point scale from "better" to "worse."

Results

A total of 77 patients was seen in the clinics, of whom 57 (74%) were men and 20 (26%) were women. The average age was 41 years. Sixty-five per cent of the patients were married and 70% were employed. Approximately one-third of the referrals were made through the family physician; about 10% each were self-referred, referred from courts, and referred from other social agencies including public welfare; referrals from relatives comprised 6.5% and from Alcoholics Anonymous, 3.9%; and the remainder represented miscellaneous multiple sources of referral.

Treatment included both individual and group psychotherapy. Duration of treatment varied from 2 to 37 weeks, the average being 19 weeks. The average number of treatment sessions per patient was 10.3. Group patients remained in treatment for an average of 16.7 sessions, whereas patients in individual treatment remained for an average of only 6.4 sessions. Approximately two-thirds of all patients attended treatment regularly, that is, they consistently kept most of their scheduled appointments. In addition, this population was unique in that in about one-half of the cases the patients' relatives had some contact with social workers and public health nurses in the clinics during the course of the patients' treatment. Though frequently brief, and not involving treatment in the traditional sense, these contacts were concerned with family problems related to drinking. It is of special interest that 12 spouses of patients were included in a more formalized treatment program.

Progress of patients in treatment in terms of the criteria mentioned previously is summarized in table 1. It is of particular significance that 51% of the patients showed improvement in family and social adjustment alone. Twenty-three per cent of the patients were reported by their therapists to have improved on all four of the criteria employed; 19% improved on three of the four criteria; 12% on two criteria; 15% on one criterion; and 32% showed no improvement on any of the four criteria. The fact that 42% of the patients improved on three or more of the criteria is indicative of the substantial therapeutic progress of the patient population.

Table 2 shows the relationship between improvement on one or more criteria and the amount of treatment. The population was divided into those patients who had eight or more therapy sessions and those who had less than eight. Of the patients who had eight or more sessions 80% improved on two or more of the four criteria. In contrast to this group, only 26% of those with less than eight sessions of treatment showed improvement on two or more criteria. The significance of the relationship between length of treatment and improvement on the multiple criteria is highlighted by the fact that 53% of the patients with less than eight treatment sessions did not show improvement on a single criterion.

It is recognized that the improvement noted above may be only of a temporary nature, and a follow-up study would be necessary to ascertain the permanence of these positive changes. Nevertheless, the findings of this cross-sectional study seem to warrant the conclusion that a favorable response to treatment was demonstrated.

TABLE 2.—*Relationship Between Amount of Treatment and Improvement Criteria**

Criteria Showing Improvement	Patients				Total No.
	0-7 Sessions		8 or More Sessions		
	No.	%	No.	%	
0 or 1	25	74	7	20	32
2 to 4	9	26	28	80	37
Totals	34	100	35	100	69

* Data on all four criteria available only for 69 of the 77 patients in survey population. Chi-square = 19.9, $p<0.001$.

As noted previously, the ratio of male to female patients was approximately 3:1. Even though the female patients attended fewer sessions than did the men, they showed a slightly greater trend toward improvement. This improvement consisted of positive change on more of the four criteria than was true for the males and included greater reduction in drinking. Fifty-nine per cent of the women showed improvement on three or more of the criteria as compared to only 37% of the men. Approximately twice as many men as women showed no improvement on even a single criterion. Table 3 summarizes the amount of improvement in relation to patient's sex and to participation or nonparticipation of patient's spouse.

TABLE 3.—*Relationships Between Sex of Patient, and Participation or Nonparticipation of Spouse in Concurrent Therapy, and Improvement*

Patients		Treatment Sessions, Mean No.	Drinking, Mean Amount*	Percentage Showing Improvement on Criteria†‡				
Type	No.			4	3	2	1	0
Women	20	10.3	1.1	29.4	29.4	17.6	5.9	17.6
Men	57	14.6	1.7	21.1	15.4	9.6	17.3	36.5
With spouses in treatment	11	12.3	0.7	46	27	18	...	9
Without spouses in treatment ..	58	13.5	2.1	19	17	10	17	36

* Lower score = more positive change, e.g., 0.0 = abstinence.

† Because frequencies in several categories were quite low, categories 3 and 4 and 0-2 were combined.

‡ For the data comparing women and men, chi-square = 2.69, $p < .20$. For the data comparing patients with and without spouses in concurrent treatment, chi-square = 5.06, $p < .05$.

In half of the clinics a limited number of spouses was involved in active treatment in addition to that being given to the patients. Although complete data were available on only 11 of the spouses involved in treatment, this number was sufficient to permit a comparison of improvement on the four criteria between patients whose spouses were included in concurrent treatment and the remaining population. The improvement rate of patients whose spouses were also in therapy far exceeds that of the remaining population, even though the average number of treatment sessions for each of these groups was approximately the same. Of equal importance is the fact that patients whose spouses were in treatment showed greater reduction in amount of drinking. As can be seen in table 3, 73% of the patients whose spouses were in treatment evidenced improvement on three or more of the criteria in contrast to only 36% of the patients whose spouses were not in treatment. The higher quality of improvement can be seen by the fact that 46% of the patients with spouses in treatment showed improvement on all four criteria. Of those whose spouses were not in treatment only 19% showed improvement on all four criteria. Moreover, the improvement of the patients whose spouses were in treatment exceeded the levels achieved on these four criteria by the male and female patients taken separately.

The importance of active concurrent treatment of the spouse is further demonstrated in table 4. Complete data were available for 13 patients whose spouses had routine social service contacts. These were compared with those patients whose families did not receive social service attention and whose spouses were not in concurrent therapy. As can be seen, there is a suggestion of greater reduction in drinking for the 13 patients cited above. Almost three times as many patients with social service contacts showed improvement on all four criteria. However, when the data are analyzed as in table 3, no difference between these two populations is apparent. The effect of social service contacts on improvement appeared to be greater in the population receiving such service, but the improvement was less than that observed in the patients whose spouses had active, concurrent treatment.

Comment

Treatment of chronic alcoholism remains a major public health problem for which no reasonably effective approach has been developed. The analysis of the community-sponsored alcoholic rehabilitation clinics in Maryland has afforded an opportunity for appraising one of the increasingly popular means of coping with this problem as a first approximation to obtaining data for future program planning.

The three major factors contributing to favorable response to clinical treatment of chronic alcoholism described above raise important issues relative to the patterning of therapy for such patients. The first of these pertains to the nature of the population attracted by community outpatient clinics. As has already been reported,[1] these patients tend to be married and employed. Similarly, the population under study manifested more than the expected social stability and was in extreme contrast to the alcoholic stereotype. Perhaps the large proportion of this kind of alcoholic patient accounts for the substantial periods of therapy duration, regularity of attendance, and high rate of improvement achieved by patients in this study. Certainly these results were contrary to what was anticipated and compare favorably with other types of outpatient populations.[2] The "skid row" stereotype of the alcoholic may have so dominated our thinking that we have been led to underestimate the potential for improvement of the majority of patients who actually seek treatment. This highlights the need to change some of the older concepts pertaining to alcoholic patients, at least those who appear in clinics for help.

TABLE 4.—*Attendance and Improvement of Patients With and Without Social Service Contacts**

Patients		Treatment Sessions, Mean No.	Drinking, Mean Amount†	Percentage Showing Improvement on Criteria‡				
Type	No.			4	3	2	1	0
With social service contacts ...	13	17.5	1.7	38.5	...	15.4	15.4	30.7
Without social service contacts	45	12.2	2.1	13.3	22.2	8.8	17.6	37.8

* Patients with spouses in concurrent treatment are excluded for this comparison.

† Lower score = more positive change, *e.g.*, 0.0 = abstinence.

‡ Because frequencies in several categories were quite low, categories 3 and 4 and 0-2 were combined. The chi-square test is not significant.

Apparently something in the structure of the clinic attracts a certain group of alcoholic patients favorably disposed to treatment. Conceivably, the existence of these alcoholic rehabilitation clinics in a familiar agency, the health department, which already provides a broad range of preventive as well as clinical services for the family, positively influences the use of and response to these services by the patients. The fact remains that such a group of patients possesses the potential for improvement and the physician must determine those factors relevant to successful clinical treatment.

The second of the findings emphasizes one of the important factors in the recovery of these patients; namely, concurrent treatment of the family, in this case the spouse. One of us[3] has already pointed out some significant contributions of family-oriented treatment for chronic alcoholics. The involvement of the spouse has also been suggested by several other workers.[4] These investigations emphasize alcoholism as a family problem, and the implication is clear that recovery should be sought in the context of the family.

In the present investigation, patients whose spouses were in active concurrent therapy showed a significantly superior improvement in both quality and amount of change. Whether this is due to factors within the patient, the spouse, or both cannot be stated at this time, but it does seem clear that excessive drinking in a family involves more than the drinker alone. The total picture must be taken into consideration within the framework of therapy to facilitate improvement. It is also reasonable to assume that such concurrent treatment will have beneficial effects on other members of the family not immediately involved in the therapy process. Unpublished data recently gathered by us indicate the presence of an alcoholic parent in at least 25% of a group of approximately 100 psychoneurotic outpatients seeking therapy at the Henry Phipps Psychiatric Clinic of Johns Hopkins Hospital. Increased efforts at family treatment should have preventive effects on children growing up with parents who have drinking problems. Moreover, the patients whose relatives received routine social service contacts showed more improvement than those who did not receive such contacts, but less improvement than those whose spouses were in concurrent therapy. This further demonstrates the importance of active concurrent involvement of the family in the patient's recovery process.

The last important finding is that group therapy was possibly more acceptable and more advantageous to these patients than individual therapy. Group patients remained in treatment for more than twice as many sessions as patients in individual therapy. Indirectly associated with this is the finding that, on the whole, improvement depends on total amount of treatment. It is our impression that greater exploitation of the group approach, not only for patients but for spouses and family as well, should be given consideration in future planning of rehabilitation programs for chronic alcoholic patients. One of us[5] has pointed out some of the theoretical aspects of group therapy for chronic alcoholics which make it an advantageous form of treatment for this kind of population.

Summary and Conclusions

Evaluation of the Maryland alcoholic rehabilitation clinics revealed that a group of patients who were married and employed were attracted by the services offered. These patients were not essentially different in many characteristics from other psychiatric outpatients. Patients attended regularly for substantial periods of time and with good results. As a consequence of this study, it seems wise to investigate the factors in the community clinic approach which facilitate the recovery of this special population. Involvement of the family in concurrent therapy and group methods of treatment were related to the excellent response in terms of improvement shown by these patients. From this it is concluded that future planning for the outpatient therapy of chronic alcoholic patients should move in the direction of greater use of techniques which involve the family, including the establishment of family-type clinics and greater use of group treatment methods not only for the patient but also for family members.

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RHEUMATIC ENDOCARDITIS COMPLICATED BY TYPHOID

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Laboratory findings can provide an early diagnosis of coexistent rheumatic heart disease and typhoid. A boy 12 years of age was hospitalized because penicillin and sulfonamide compounds failed to control a week-long episode of fever, chills, headache, nausea, and nonproductive cough. He had had rheumatic heart disease (with aortic stenosis and mitral insufficiency) four years before the admission; at the time of admission he had a fever and slow pulse rate. The cardiac state was unchanged as compared to previous examination. Absence of anemia and absence of elevated sedimentation rate and leukocyte count cast doubt on presence of either active rheumatic fover or subacute bacterial endocarditis. A gram-negative bacillus was found in the blood culture. The agglutination reaction was positive for typhoid O agglutinins. The patient was treated for and cured of typhoid with a total of 33.5 Gm. of chloramphenicol over a period of 18 days. No sequelae developed within the subsequent four years.

The early recognition of any bacteremia in a patient with rheumatic heart disease is of utmost importance. A case of rheumatic heart disease complicated by typhoid is reported because of several interesting features: 1. The coexistence of these disorders is extremely rare.[1] 2. The differential diagnosis is more than an academic exercise, because it is vital to proper therapy.[2] Early and adequate specific treatment may be rewarded by cure of the patient, whereas delay or improper treatment may result in a fatal subacute bacterial endocarditis due to a salmonella organism[3] or death may ensue from the ravages of typhoid itself.

Report of a Case

A 12-year-old boy was first seen in February, 1950. He was known to have had heart murmurs since he was 4 years of age. Although there was no classic history of rheumatic fever, the child was described as having aching legs and "growing pains." Of significance also in the history was the fact that two cousins had had rheumatic fever.

On physical examination the pertinent abnormal findings were limited to the heart and consisted of a grade 3 harsh aortic systolic murmur with a thrill and a grade 2 harsh mitral systolic murmur transmitted to the axilla. The mitral first sound was accentuated, and the pulmonic second sound was louder than that of the aortic second sound.

On fluoroscopy there was noted slight enlargement of the left ventricle, but all other chambers appeared normal. The electrocardiogram was normal, and findings on routine hemogram, sedimentation rate determination, and urinalysis were likewise normal. The diagnosis of rheumatic heart disease with aortic stenosis and mitral insufficiency was made. On subsequent yearly visits there was no change in his cardiac status.

On Jan. 23, 1954, I was asked to see the patient at his home and obtained the following history. He had been seen by a physician one week previously because of fever, chills, headache, nausea, and a nonproductive cough of two days' duration. He was given penicillin both parenterally and by mouth. When the fever and chills persisted two days later, sulfonamide drugs were also prescribed. The mother added aspirin each time the temperature went over 101 F (38.3 C), and she stated that this seemed to be the only thing that brought the temperature down but it became elevated again within a few hours. At the time of my examination the only subjective symptoms were anorexia and headache. Physical examination showed the temperature to be 101 F, the pulse rate slow and of good volume, and the cardiac findings essentially unchanged from previous examinations; there were no other significant physical findings. I suggested that the patient be hospitalized, because it was impossible at that time to determine whether he had a recrudescence of rheumatic fever, subacute bacterial endocarditis, or some other febrile disease or infection. The patient was, therefore, admitted to the Presbyterian Hospital, Newark, N. J.

On admission the temperature was 101.8 F (38.7 C), the pulse rate 90 per minute, and respirations 24 per minute. He was immediately given 15 grains (970 mg.) of aspirin, and an order was left for that amount to be given every four hours. It is common knowledge that recurrences occur in 30 to 50% of patients with rheumatic fever after a streptococcic infection,[4] and this may be so slight as to be clinically overlooked. Also, active rheumatic fever may rarely occur with a relative bradycardia.[5]

On Jan. 24 the temperature at 8 a. m. was 103.8 F (39.9 C) in spite of the aspirin. On examination, there were no localizing physical signs and one could not help but comment on the slow pulse rate relative to the height of the temperature.

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An electrocardiogram obtained that morning showed regular sinus rhythm with a ventricular rate of 88 per minute, P-R interval 0.12 seconds, and QRS complex 0.06 seconds. Thus, there were no electrocardiographic abnormalities. Meanwhile, blood was drawn for a hemogram, heterophil agglutination test, sedimentation rate, and agglutination tests for typhoid, paratyphoid, Brucella, and Proteus OX$_{19}$. Blood for cultures was drawn at noon, 4 p. m., 8 p. m., and midnight. A routine urine study was done, and urine for culture was taken.

The results of urinalysis, sedimentation rate determination, and blood cell count were reported as follows: urine: specific gravity 1.012, 8-10 leukocytes per high-power field, and other findings normal; hemogram: hemoglobin level 14 Gm. per 100 ml. (84%), red blood cell count 4,460,000 per cubic millimeter, and white blood cell count 6,100, with 31% segmented neutrophils, 4% monocytes, 6% stab cells, 1% eosinophils, and 58% lymphocytes (a rare atypical lymphocyte was seen); and sedimentation rate 8 mm. per hour (Westergren).

These findings tended to cast doubt on the diagnosis of active rheumatic fever and the existence of subacute bacterial endocarditis because of the absence of anemia and the lack of elevation of the sedimentation rate and the leukocyte count. Salicylates, however, will depress the sedimentation rate to some extent.[6]

The next day, two days after his admission, the temperature remained elevated and the pulse rate slow and the patient complained of pain in the left elbow which was tender on movement but was without redness or swelling. He appeared lethargic, but there was otherwise no change in physical findings. On this day the following laboratory reports were returned: heterophil agglutination positive in a 1:7 dilution, typhoid H agglutinin positive in 1:80 dilution, typhoid O agglutinin positive in 1:320 dilution, paratyphi A negative in all dilutions, Brucella abortus negative, and Proteus OX$_{19}$ negative. The blood culture taken at noon the previous day showed no growth. The 4 p. m., 8 p. m., and midnight specimens, however, showed a gram-negative bacillus. With this presumptive evidence of salmonella infection the patient was started on chloramphenicol (Chloromycetin) therapy.

The next day, three days after admission, the patient was still febrile and had rose spots on the abdomen and lower thorax anteriorly and the tip of the spleen was palpable. A second hemogram showed about the same hemoglobin level and red blood cell count, but the white blood cell count was 4,220 per cubic millimeter. Agglutination reactions at this time showed a rising titer of typhoid O agglutinins, which was now positive in a dilution of 1:640. Specific serum had established the diagnosis by a positive agglutination of the organism obtained on culture.

The next day the patient was transferred to the Essex County Isolation Hospital at the request of the board of health. Follow-up studies showed the titer for typhoid O agglutinin had risen to 1:800. Urine and stool cultures were, however, negative during the complete course of the disease, no doubt due to the specific treatment.

There were many questions that gave food for thought. Had the typhoid bacillus implanted itself on the damaged valves? After all, bacteremia and susceptible valves, the two conditions necessary for subacute bacterial endocarditis, were present. How long must treatment continue, and what are the accepted doses of chloramphenicol in this type of case?

Both answers were based on the treatment of typhoid itself rather than on the coexistence of the two diseases. In 18 days of treatment the patient had a total dosage of 33.5 Gm. of chloramphenicol. Stool cultures on three successive days after this treatment were negative, and the patient was then discharged as cured of typhoid. He has shown no sequelae after four years.

Comment

The differential diagnosis of prolonged fever in a patient with rheumatic heart disease includes not only active rheumatic fever and subacute bacterial endocarditis but also unrelated infectious diseases, collagen vascular diseases, neoplastic diseases, especially lymphomas, blood dyscrasias, and drug reactions.[7] This case demonstrates the need for a thorough diagnostic study in such patients before embarking on a program of prolonged treatment for subacute bacterial endocarditis without a positive culture.

It is interesting to note that subacute bacterial endocarditis and typhoid have many nonspecific features in common, namely, headache, malaise, chills, fever, cough, sweats, a skin rash, abdominal pain, palpable spleen, anemia, and arthritis or arthralgias. Definitive laboratory studies provide the differential diagnosis.

Summary

In a rare case, rheumatic heart disease was present with typhoid. Early diagnosis of bacteremia in patients with chronic rheumatic valvular disease is important.

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ARTERENOL THERAPY FOR SHOCK AFTER ACUTE MYOCARDIAL INFARCTION AND PULMONARY EMBOLIZATION

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and

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A study was made of the records of 55 patients who had severe shock after myocardial infarction and who were treated with either arterenol or metaraminol bitartrate. A distinct pressor effect was obtained in 42, shock was relieved in 38, and seven-day survival followed in 22. A similar study was made of 11 patients with shock after pulmonary embolism who received the same treatment. A distinct pressor effect was obtained in seven, shock was relieved in five, and seven-day survival followed in three. It is recommended that treatment with arterenol be started promptly after the recognition of shock in either type of patient. The simultaneous use of digitalis products in patients with coexistent congestive heart failure was not found harmful. To prevent local tissue injury, which caused sloughing in three cases, the bottle containing arterenol should be attached to the venoclysis apparatus only after a free flow has been established with a 5% solution of dextrose in water.

Arterenol (norepinephrine [Levophed]) is a naturally occurring substance which is the adrenergic nerve transmitter.[1] Kaindl and Lindner,[2] in 1950, and Liljedahl and Norlander,[3] in 1951, each reported its successful use in one patient with shock after myocardial infarction. Birke,[4] in 1952, published the results on three patients. In the United States, Miller and Baker [5] and Kurland and Malach [6] also presented their studies in 1952. These initial papers served to establish the relative safety of arterenol in the treatment of shock after myocardial infarction, and subsequently a number of other studies, some of which are summarized in table 1, have appeared.

In 1953, Miller and co-workers [7] reported the successful use of arterenol in two patients in shock after pulmonary embolization. Subsequently a few additional such patients were reported.[8]

It is now almost uniformly agreed that the therapy of choice for cardiogenic shock includes the use of vasopressor agents. An important impetus to this thinking was the report on mephenteramine by Brofman and associates.[9] In our view, arterenol is the vasopressor of choice when dealing with such a grave condition as severe shock after myocardial infarction, but its use needs considerable further clinical evaluation.

The present report summarizes a one-year experience of consecutively treated patients with cardiogenic shock at the Michael Reese Hospital, Chicago. Also, data on 11 additional patients with shock after acute pulmonary embolization are presented.

Methods and Criteria

The case histories of patients treated for shock with vasopressor drugs during a one-year period (August, 1956, to August, 1957) were collected. The records of the hospital pharmacy were used, and every patient who received arterenol or metaraminol bitartrate was noted. The hospital record was then reviewed and the data summarized.

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In this period, a total of 123 patients were treated for shock with arterenol, metaraminol, or both. Fifty-five of them fulfilled our criteria for having severe shock after myocardial infarction; 11 patients fulfilled similar criteria for shock after pulmonary embolization. The results in these two groups of patients form the basis of this report.

Our criteria to define severe shock are similar to those recommended by Binder and associates[10]: (1) systolic blood pressure 80 mm. Hg or less, (2) the presence of clinical signs of peripheral circulatory collapse, and (3) failure to respond to therapy which effectively relieved pain. However, in those patients known to have had hypertension previously, a systolic blood pressure of 90 mm. Hg or less was used instead. The pulse rate was not used in defining severe shock. We included patients with heart failure and arrhythmias and did not exclude those patients who died within one hour after therapy was started; the latter were analyzed separately.

In all instances, the diagnosis of acute myocardial infarction was confirmed by electrocardiogram or autopsy. The diagnosis of acute pulmonary embolus was made on clinical grounds, with electrocardiographic support and, in some instances, confirmation by autopsy.

A satisfactory pressor response was defined as a rise to a systolic blood pressure of 100 mm. Hg or higher. The shock was considered relieved if, after a satisfactory pressor response, the clinical signs of peripheral circulatory failure disappeared whether or not arterenol was still being administered. "Survival" was considered to have occurred when the patient lived for one week after arterenol therapy was discontinued. Note was made of patients who lived for 24 hours after therapy was instituted, whether or not arterenol was still being used.

Table 1.—*Reports of Arterenol Therapy for Shock After Myocardial Infarction*

Year	Author	Total No. of Patients	Pressor Effect, No.	Relief of Shock, No.	Survived, No.	Died, No.
1950	Kaindl and Lindner[2]	1	1	1	1	0
1951	Liljedahl and Norlander[3]	1	1	1	1	0
1952	Birke[4]	3	3	3	2	1
1952	Miller and Baker[5]	7	4	1	1	6
1952	Kurland and Malach[6]	14	10	9	4	10
1953	Livesay and Chapman, cited by Binder and others[10]	6	5	1	1	5
1953	Miller and others[7]	9	8	5	5	4
1953	Gazes and others, cited by Binder and others[10]	7	7	7	6	1
1953	Smith and Guz, cited by Binder and others[10]	6	6	4	4	2
1953	Calenda and others, cited by Binder and others[10]	13	9	4	2	11
1953	Moyer and others, cited by Binder and others[10]	14	12	6	6	8
1954	Sampson and Zipser[11]	30	27	20	16	14
1954	Binder and others[10]	25	23	12	8	17
1957	Littler, T. R., and McKendrick, C. S.: Lancet 2:825, 1957	22	10	..	0	22
	Total	158	126 (80%)	74 (46%)	57 (36%)	101 (64%)

Results

Shock After Myocardial Infarction.—The over-all mortality in the cases collected from the literature (table 1) was 64%. The over-all mortality in our present series was 60% (table 2). When the patients who received arterenol therapy for less than one hour before death are omitted, the mortality becomes 49%. This is close to that obtained by Sampson and Zipser[11] and represents a marked improvement over the known grave prognosis of cardiogenic shock not treated with vasopressor drugs.[12]

Table 2.—*Results of Arterenol Therapy in Fifty-five Patients with Shock After Acute Myocardial Infarction*

	No.	%
Pressor effect	42	76
Relief of shock	38	70
Survived		
24 hr.	31	56
Total	22	40
Died		
1 hr.	12*	22
Total	33	60
Frank congestive heart failure	13	24
Hypertension prior to shock	12	22
Auricular fibrillation	7	13
Atrioventricular dissociation	4	7

*Eleven were designated as "preterminal" on hospital chart and died within one-half hour after arterenol therapy was started.

The patients ranged in age from 44 to 91 years. Sixteen patients had a history of one previous myocardial infarction and two others of two such episodes. There was no significant difference in the results of treatment between those patients with and without a history of previous myocardial infarction. However, congestive heart failure significantly worsens the prognosis, as has been observed by others.[10] Thirteen patients had congestive heart failure; two of them survived.

The duration of shock, as expected, does influence treatment results. Three of 10 patients, in whom the shock was known to have been present for four hours or longer when treatment was started, survived. Ten of 17 patients treated when the shock was present for less than one hour survived. A history of previous hypertension did not significantly alter the results in our series.

All patients in frank congestive heart failure received one or another digitalis product. The results do not show any particular trend. In a number of instances the patients were not fully digitalized. In no case did the combination of digitalization and arterenol therapy appear harmful, an observation in keeping with our previous experience.[7]

Hydrocortisone was used in only four patients, with no demonstrable effect on the shock. Three of the 55 patients received metaraminol. No discernible effect was present in two patients; in the other, the blood pressure was adequately maintained subsequent to the relief of shock with arterenol.

In general, our experience in this series confirms previous observations[10] that the amount of arterenol administered per unit of time is of prognostic significance. However, two patients with satisfactory pressor responses to a modest dosage of arterenol subsequently were found to have massive myocardial infarction at autopsy.

Three of four patients with advanced atrioventricular block died. Five of the seven patients with auricular fibrillation died. All of the patients with auricular fibrillation received a digitalis product.

Shock After Acute Pulmonary Embolization.—The results of arterenol therapy for shock after acute pulmonary embolization are given in table 3. Five of the 11 patients were treated postoperatively. Five patients died less than one hour after the institution of arterenol treatment.

Complications.—Three of the 66 patients treated had superficial skin sloughs after infiltration by the arterenol solution. No skin grafting was necessary.

Comment

This retrospective study confirms the general opinion previously expressed in the literature, namely, that vasopressor therapy significantly improves the prognosis when shock complicates acute myocardial infarction. Manifest congestive heart failure plus shock remains a grave prognostic combination, and, when present, the results with arterenol are poor. A number of patients in our series were inadequately digitalized. Inasmuch as there appears to be no problem in using arterenol and digitalis products simultaneously, we strongly urge that digitalization should be adequate whenever congestive heart failure, even when slight in degree, is manifest. Indeed, the prognosis is in such cases so poor that rapid intravenous digitalization is probably advisable. Griffith and co-workers [12a] were unable to demonstrate a potentiating effect of hydrocortisone on the vasopressor action of arterenol when treating shock. Though we have noted no response in four patients, further investigation is necessary.

Table 3.—*Results of Arterenol Therapy for Shock After Acute Pulmonary Embolization*

Year	Author	Total No. of Patients	Pressor Effect, No.	Relief of Shock, No.	Survived, No.
1953	Miller and others [7]	2	2	2	2
1954	Wolff [8a]	1	1	1	1
1955	Sibthorpe [8b]	1	1	1	1
1955	De Swiet [8c]	1	1	1	1
Present study		11*	7	5	3
Total		16	12	10	8(50%)

* Five who died were treated less than one hour before death.

Shock after myocardial infarction should be treated as early as possible. Procrastination in instituting vasopressor therapy significantly decreases the survival rate. Indeed, serious consideration must be given to the use of vasopressors when hypotension persists after pain has been relieved. In such circumstances, the use of phenylephrine, mephentermine or metaraminol is satisfactory. When severe shock is present, the use of arterenol is preferred, since this drug's high potency is not matched by any other pressor agent. A substantial body of data indicates its high degree of safety. However, all potent vasopressor drugs should be used with caution in patients receiving vagal blocking drugs, since previous work from this department [13] has shown that arterenol administered under these circumstances may lead to supraventricular arrhythmias.

The use of arterenol has been criticized because it requires administration under constant medical supervision. However, patients in severe shock must be under constant medical surveillance irrespective of the therapy being used. In the presence of severe shock, intravenous therapy, insuring the immediate delivery of the drug, is obviously desirable.

Arterenol may cause local tissue injury, this being a reflection of its extreme potency as a vasoconstrictor agent. It is our impression that local tissue sloughs sometimes result from infiltration when the intravenous drip is being started. Accordingly, the bottle containing arterenol should be attached only after a free flow has first been established with a 5% solution of dextrose in water. Phentolamine (Regitine) hydrochloride should be injected locally whenever arterenol solutions infiltrate subcutaneously.[14]

No clear conclusions can be reached from the relatively few treated patients with shock after acute pulmonary embolization reported to date. Much further experience is needed in the use of vasopressor therapy. Certainly vasopressors merit consideration in this grave clinical condition.

Summary

A retrospective evaluation of arterenol (norepinephrine [Levophed]) therapy for shock after acute myocardial infarction and acute pulmonary embolization was based on a one-year experience at the Michael Reese Hospital, Chicago. Fifty-five patients with shock after myocardial infarction and 11 with shock after pulmonary embolization were studied. Arterenol was seen to be the therapy of choice in severe cardiogenic shock, and it significantly improves the prognosis. Manifest congestive heart failure along with shock after myocardial infarction remains a grave combination. Full digitalization, preferably by the intravenous route, should accompany arterenol treatment under these circumstances.

As with other forms of shock, the earlier treatment is begun the more effective it becomes. Hypotension persisting after the pain of acute myocardial infarction has been relieved may require treatment. Vasopressor drugs which can be administered subcutaneously or intramuscularly should be effective in most such instances. More data are needed on shock complicating pulmonary embolization before definite conclusions on the effectiveness of vasopressor therapy in this condition can be drawn.

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BENIGN NEOPLASMS OF THE SMALL INTESTINE

WITH A REPORT OF THREE BLEEDING BENIGN TUMORS OF THE JEJUNUM

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Three cases are described in which patients were hospitalized for massive intestinal bleeding. In each case the results of roentgenography were either negative or misleading, and the preoperative diagnosis was a probable bleeding duodenal ulcer, although the presence of tumor was considered. One patient also showed signs of intussusception. At laparotomy in each case the lesion proved to be a benign tumor, and excellent results followed resection. These observations are in accord with existing records of more than 1,400 cases of benign tumors in the small intestine. Many are asymptomatic, and less than 8% of all patients in whom such lesions were found by the surgeon had been given diagnoses before operation.

Although benign tumors of the intestine are admittedly uncommon, they can no longer be considered rare.[1] They are being reported with increasing frequency due to newer x-ray techniques, as well as to a greater awareness of their presence. The total number of documented cases exceeds 1,400. This does not include ectopic inclusions in Meckel's diverticula, aberrant tissues such as in the pancreas and gastic mucosa, hematomas, plasma cell myelomas, endometrial carcinomas, granulomas, inflammatory polyps, or carcinoids. With the exception of carcinoids, these are not true tumors, and the latter are of very questionable benignancy.

In most series, benign tumors of the small intestine are found to be less frequent than malignant ones, averaging 30 to 45% of the total.[2] In the younger age groups, however, the benign tumors apparently outnumber the malignant ones.[3] The malignant tumors occur in a somewhat older age group, the patients averaging 47½ years, as compared with 38 years for those with benign tumors.

Since the symptomatology of the benign lesions is frequently mild and nonspecific, the diagnosis is difficult to establish. Even when laparotomy is considered necessary, the preoperative diagnosis is seldom more than suspected. In symptomatic lesions, repeated laparotomies have, on occasion, been necessary before the lesion was discovered. Many tumors are found incidentally at surgery or at autopsy.

Many of the reports on smaller series state that the majority of benign tumors are found on postmortem examination.[4] However, the most authoritative review of the subject, by River, Silverstein, and Tope,[2c] reveals that in 72% of the 1,399 cases collected from the world literature through 1954 the tumors were removed at the time of surgery.

Etiology

The ultimate cause of most neoplasms is unknown, but the etiology of those in the small intestine is perhaps open to more speculation than elsewhere. Morison[5] commented in 1941 on the "remarkable immunity" of this region to neoplasms. This is despite the fact that the small intestine makes up 75% of the alimentary tract; it is more remarkable because the small intestine is preceded and followed by the stomach and colon, respectively, wherein 40% of all malignant growths originate. Less than 0.5% of all gastrointestinal carcinomas occur in the small intestine. Benign growths, however, are relatively more common; about 25% of the total benign gastrointestinal tumors occur in the small intestine.[6]

Numerous reasons for the low incidence of new growth in this region have been postulated. The most widely accepted of these hypotheses are (1) the alkalinity of the intestinal contents, (2) the minimum of stasis and kinking in this region, and (3) the diminished trauma due to the liquid nature of the fecal stream.[7] The etiological factor in certain cases apparently is hereditary, as evidenced by anobuccal melanosis (Peutz-Jeghers), neurofibromatosis (Recklinghausen's disease) involving the intestine, and certain cases of intestinal telangiectasia due to hemangiomatosis (Rendu-Osler-Weber) syndrome. In addition, certain other cases suggest a familial tendency. In some patients requiring multiple operations, the tumors are of different types, suggesting a low resistance to neoplasms.

According to River and co-workers,[2c] the sex incidence of these tumors is approximately equal, and the majority (60%) occur in persons between the ages of 30 and 60. However, almost 15% were in patients under 20, and about 0.1% of the total occurred in patients below one year of age.

Sarcoma is relatively more common than carcinoma. In fact, the majority of gastrointestinal sarcomas actually occur in the small intestine.[8] This suggests, perhaps, that sarcoma occurs somewhat as a happenstance, related more to the total length of the intestine exposed than to any specific etiological factor. This may also be true, to a lesser extent, of the benign tumors.

Pathology

Seventy-five per cent of the benign tumors of the small intestine, in their relative order of frequency, are adenomas, lipomas, myomas, polyps, fibromas, angiomas, or hemangiomas. It is noted that about two-thirds of the total originate from connective tissue.[2c]

The relative percentages of malignancy, as well as the incidence of all tumors, increase from the duodenum and jejunum to the ileum, being about 18, 25, and 57% respectively.[2c] These percentages are proportional to the lengths of the individual segments, although the jejunum may have somewhat less than its share.

The majority of benign tumors tend to be intraluminal, although they may be intramural or subserosal, depending on the site of origin.[4] As growth occurs in the intramural variety, they usually present as subserosal or intraluminal tumors. The majority of benign tumors are polypoid, although they may partially or completely encircle the intestine on occasion, as the malignant growths frequently do. Their polypoid nature accounts in part for the high incidence of intussusception with benign tumors, although this finding is uncommon with malignancy. The infrequency of intussusception with malignancy is also due to the greater induration and infiltration locally, preventing the intussusception from forming. The microscopic picture is frequently mixed in the case of connective-tissue tumors, particularly fibromas, although the epithelial lesions are usually more typical.[4]

Clinical Findings

As has been mentioned, many of the lesions never cause symptoms during life, or else the symptoms are so vague that the diagnosis is never established. The symptoms of duodenal and upper jejunal tumors frequently simulate disease of the stomach, duodenum, or pancreaticobiliary tract. Lesions of the ileum may suggest disease of the colon.[9]

The most common single condition leading to the diagnosis of benign tumors is intestinal obstruction. This is the presenting symptom in two-thirds of all cases, three-fourths of these being due to intussusception.[10] It is manifested by the usual symptomatology, with colicky pain, distention, constipation, and vomiting; if the obstruction is due to intussusception, there is frequently a palpable sausage-shaped mass and perhaps bloody mucus per rectum. This latter finding accounts for the fact that many of the cases were overlooked in earlier reviews, being lost in the voluminous literature on intussusception. In adults, the majority of all cases of intussusception are due to benign tumors of the small intestine, and such tumors should be intensively searched for whenever this type of obstruction is found at operation.[2c]

Frequently the tumor is not obvious at the time of operation, and often the intussusception has spontaneously reduced, leaving only a little dilated and edematous intestine to suggest the need for closer examination. These circumstances account for the frequent history of prior attacks, each typical of temporary mild obstruction. Numerous cases have been reported in which several explorations were required before the neoplasm was finally discovered.

Tumors of the ileum are more likely to cause intussusception than those of the duodenum, where intussusception rarely occurs. This is probably due to the semifixed nature of the duodenum and to the more solid consistency of the lower intestinal contents.[2c]

The next most common symptom is intestinal bleeding, usually manifested by anemia and/or melena. About one-third of the reported cases have presented in this way, with massive bleeding occurring in about 11%. Intussusception was a concomitant finding in half of the bleeding patients. Almost all of these patients had had numerous hospital admissions and diagnostic studies, without proper diagnosis. Massive bleeding carried with it an average mortality of 14%;[10] patients at times underwent several operations before removal of the lesion. Each of the patients here reported presented with moderate to severe upper intestinal hemorrhage; all had a history of prior episodes. One, in addition, had associated intussusception. Numerous other symptoms may occur on occasion, such as postprandial fulness, persistent or periodic epigastric pain, anorexia, and weight loss. None of these, however, is sufficiently specific to give much help in diagnosis.

Definitive diagnosis is difficult and, except in one or two series, has seldom been made preoperatively. In the most authoritative report, covering almost all the reported cases, the correct preoperative diagnosis was made in only 79 (7.8%) of the 1,014 instances in which a tumor was found at operation.[2c] The diagnosis was only suspected in the three cases reported below.

An increase in correct preoperative diagnosis has parelleled the improvement in roentgenologic techniques, and x-ray remains almost the only helpful aid in the diagnosis of benign tumors. The usual upper and lower gastrointestinal studies are rarely of much help except in excluding other diagnoses, although they may aid in revealing duodenal lesions. A negative gastrointestinal series should suggest the diagnosis in the presence of melena especially when it is massive and without hematemesis. Such a situation was present in two of our cases. In the other there was some dilation of the duodenum above an obstruction that was found later to be due to intussusception.

Detail films of the small intestine, when properly done, may be of considerable value in diagnosis[11] (although in our cases they were not), particularly when made with the aid of an inlying Miller-Abbott tube. Thin barium may be injected through the tube when the balloon is stopped by the lesion. Despite the time and effort required, these special studies should be utilized in properly selected cases. If this were done, up to 50% of these cases could be diagnosed preoperatively.[12]

Treatment

The treatment of benign tumors of the small intestine is essentially surgical and is directed at total removal by the simplest method. There should be intensive preoperative treatment of the associated anemia, electrolyte disturbances, and dehydration.

If small, tumors frequently may be removed by enterotomy and either ligation at the base of the pedicle, when feasible, or diamond-shaped submucosal excision. If the tumor is larger, a limited resection with end-to-end anastomosis is usually carried out. Rarely are benign tumors of such size or location as to require more complicated treatment.

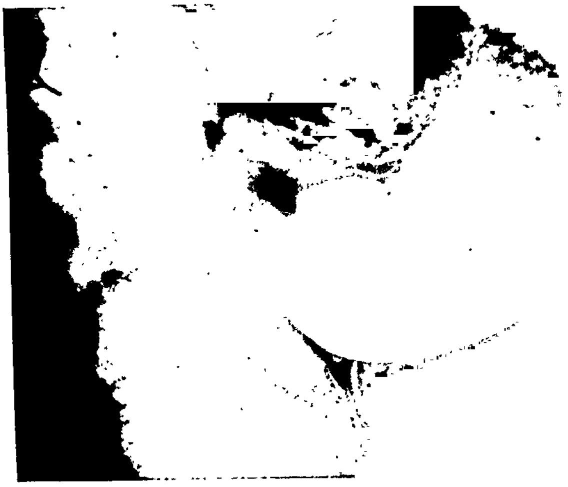

Fig. 1.—Dilated stomach and duodenum with little barium in fourth part of duodenum and none beyond duodenum.

Despite the desirability of preoperative antibiotic preparation of the intestines, most excisions have been carried out without this, with relatively good results. Tabulated results in 960 cases in one series where statistics were available, gave an over-al operative and postoperative mortality of 20.6% There has been a steady decline in mortality ove the past 20 years.[2c]

Presented below are reports on three benig jejunal tumors encountered in the practice of on of us (P. J. C.), two of them within the past yea

Report of Cases

Case 1.—A 57-year-old man was admitted on Jan. 1 1953, with the chief complaints of epigastric pain and tarr stools, both present for about three weeks. The pain in th epigastrium was described as gnawing in nature, occurrin usually when the patient was hungry and at times noctu nally. It radiated around both costal margins to the back.

was relieved by food and milk of magnesia. Simultaneously he had developed melena, which persisted in all stools. Four days prior to admission he was seen in the hospital emergency room and given medication because the pain had kept him awake. He complained of weakness during the previous week but denied syncope. There was no known weight loss, no hematemesis or other vomiting, and no diarrhea or hematochezia. He denied pyrosis and meteorism, and the gastroenterological inventory was otherwise negative, as was the remainder of the history.

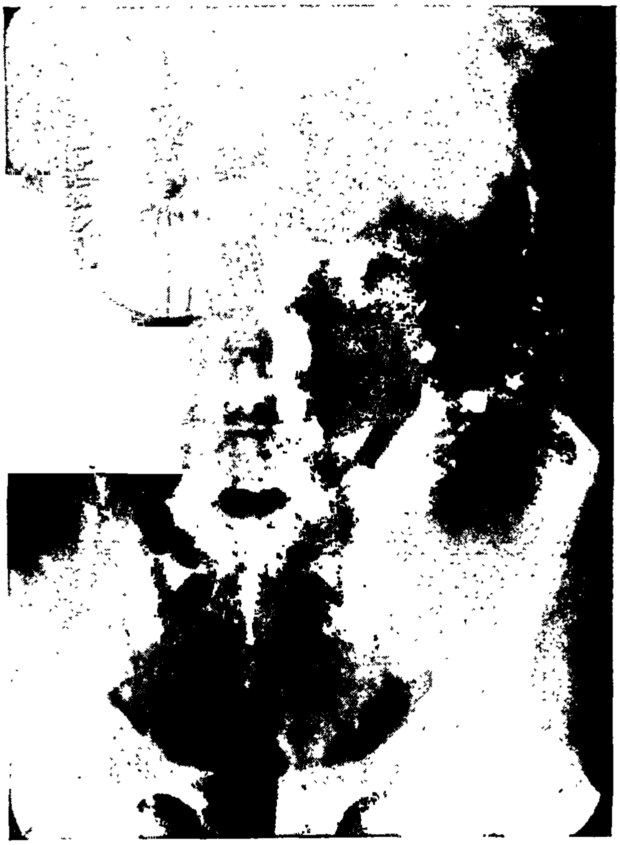

Fig. 2.—Almost complete obstruction at duodenal-jejunal junction with only trickle of barium in upper jejunum.

Three to four years earlier he had had similar pains associated with melena and was seen in another hospital, where a gastrointestinal series was reported negative. He was given a transfusion and placed on a diet for ulcers, but he discontinued this when the symptoms abated.

The patient was well developed and well nourished. He had a blood pressure of 140/80 mm. Hg, a pulse rate of 92 per minute, full and regular, and a respiratory rate of 20 per minute. The skin showed marked pallor but was dry and warm. Examination was otherwise entirely negative. The diagnosis on admission was bleeding duodenal ulcer.

Laboratory studies disclosed a hemoglobin level of 6.6 Gm. per 100 cc., a red blood cell count of 2,810,000 per cubic millimeter, and a color index of 0.77. There was marked anisocytosis and moderate hypochromia. The white blood cell count was 8,300 per cubic millimeter, with a normal differential; urinalysis was negative. Blood chemistry studies gave essentially normal results. Two days later the hemoglobin level had risen to 10.2 Gm. per 100 cc. after transfusions. There were 6.8% reticulocytes, and the platelet count was 725,000 per cubic millimeter. X-rays taken on this day revealed a complete obstruction of the third and fourth portions of the duodenum, with 100% gastric and duodenal retention at three hours (fig. 1 and 2). Studies with the barium enema gave negative results. After the upper gastrointestinal series had been completed, complete obstruction occurred. Levin tube suction was begun, and he was given fluids and blood, receiving a total of six units preoperatively, which maintained the hemoglobin level slightly below normal.

The patient was operated on eight days after admission, with the preoperative diagnosis of probable malignant duodenal tumor. Surgery revealed an intussusception about 14 in. in length, extending up to the ligament of Treitz. This was reduced by traction and pulsion. A dimpling of the wall of the jejunum was noted about 12 in. distal to the ligament, and a polyp was palpable, with a large lymph node nearby. Results of frozen section of the node were not satisfactory, so a wedge resection, including the mesenteric nodes, was done, followed by open end-to-end anastomosis. The polypoid tumor (fig. 3) proved to be a lipoma, with mucosal ulceration over the tumor. The postoperative course was uneventful, and the patient was discharged after eight days.

Case 2.—A 42-year-old woman was admitted to the hospital on Jan. 6, 1957, with the chief complaint of anemia. She had been well until one year pior to admission, when she had had a series of tarry stools without abdominal pain, hematemesis, or other gastrointestinal symptoms. She was admitted to a hospital in another city, where x-rays and sigmoidoscopic examination were reported negative. She received three units of blood and was placed on a diet for ulcers, plus iron medicaments, and was discharged.

Six months prior to the present admission she had again had a series of tarry stools associated with weakness and easy fatigability. This lasted three weeks and was associated with occasional vague abdominal discomfort unrelated to food. She was very pale on admission and her hemoglobin level was 3.2 Gm. per 100 cc., with a red blood cell count of 1,700,000 per cubic millimeter. She had 4+ occult blood in the stool, and the other laboratory studies showed normal results. She was given transfusion until her hemoglobin level reached 11.9 Gm. per 100 cc.; seven units of blood was required. A complete gastrointestinal series, including detail

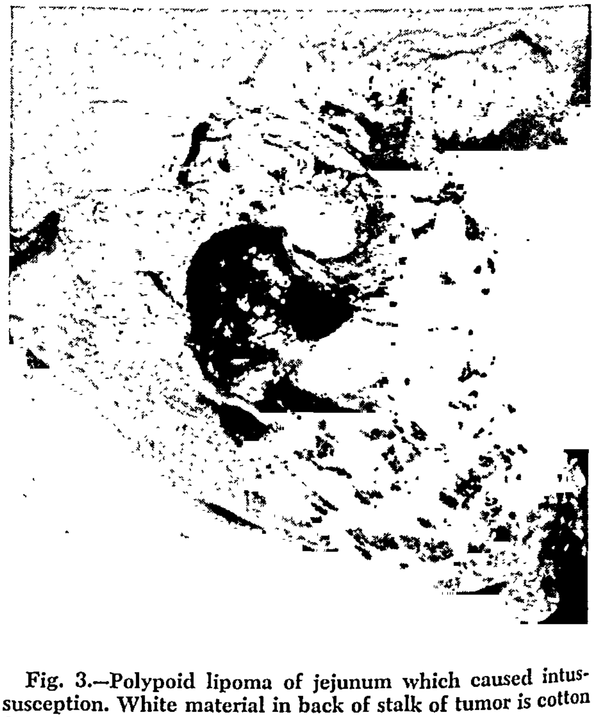

Fig. 3.—Polypoid lipoma of jejunum which caused intussusception. White material in back of stalk of tumor is cotton for photographic contrast.

studies of the small intestine, was negative. The string test was positive for blood in a localized area, 56.25 cm. from the incisors, the pylorus being estimated at 54 cm. Gastroscopic examination was refused, and she was discharged on an ulcer diet after the bleeding had apparently stopped.

The most recent admission was because a periodic examination had revealed that the hemoglobin level was again down, this time to 8.0 Gm. per 100 cc. It had been normal on previous examinations, and the patient had no melena or other symptoms, except for a loss of 20 lb. (9.1 kg.) during the previous year. She had remained on her diet. Her medical and social history, as well as the systemic review, were negative, except for a history of hypertension five to six years earlier.

The patient was obese, and her skin was quite pale. The blood pressure was 130/75 mm. Hg, and the white blood cell count and urinalysis were normal, as were the prothrombin time and platelet count. The stool contained 4+ occult blood. X-rays were again normal. The string test revealed blood staining from what was thought to be the cardia to the pylorus. Administration of six units of blood was required over a two-week period to maintain the hemoglobin at near normal levels. A diagnosis of probable duodenal ulcer was made, and operation was scheduled for Jan. 22, 1957. A polypoid tumor (fig. 4, 5, and 6) of the jejunum was removed by simple wedge resection from the antimesenteric border. The patient's course was satisfactory, and she was discharged on the seventh postoperative day. The pathological diagnosis was "fibroma with ulceration."

Case 3.—A 53-year-old woman was admitted on Nov. 20, 1957, with the chief complaint of black stools for the previous three days. She gave a history of recurrent episodes of melena over a 24-year period; these attacks had occurred every few months and had lasted an average of one to three days. She had been anemic for years, the hemoglobin level being 8.9 Gm. per 100 cc. on one known occasion. The most recent attack had consisted of frequent melanotic stools, occurring several times daily. Several of them also contained bright red blood. She had been dizzy and weak during the previous 24 hours and had had an episode of syncope the evening of admission. Several of the prior bleeding episodes had been massive, requiring transfusions. The patient denied ever having had any abdominal pain, pyrosis, meteorism, or hematemesis. She had previously had numerous gastrointestinal x-rays, and all except one were normal. This one, taken several years before, apparently had revealed a duodenal ulcer. The patient said she had been easily bruised for years, but a complete hematological study two months prior to admission was entirely normal.

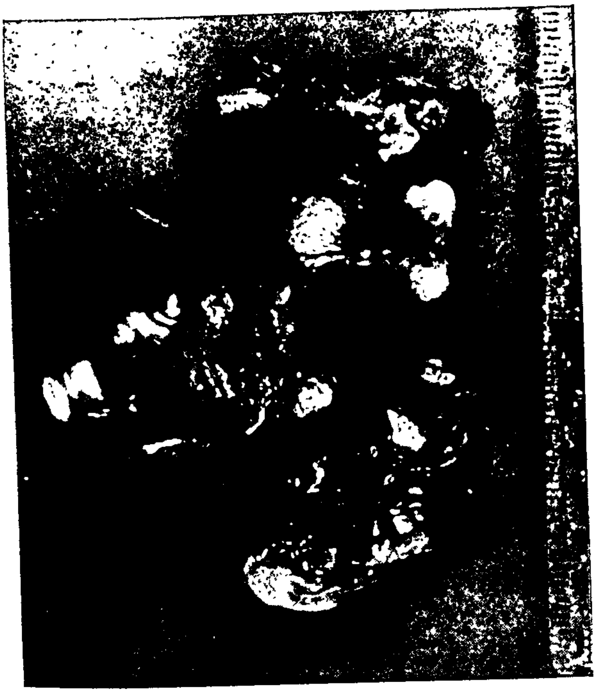

Fig. 4.—Fibroma of jejunum. Segment was removed at operation.

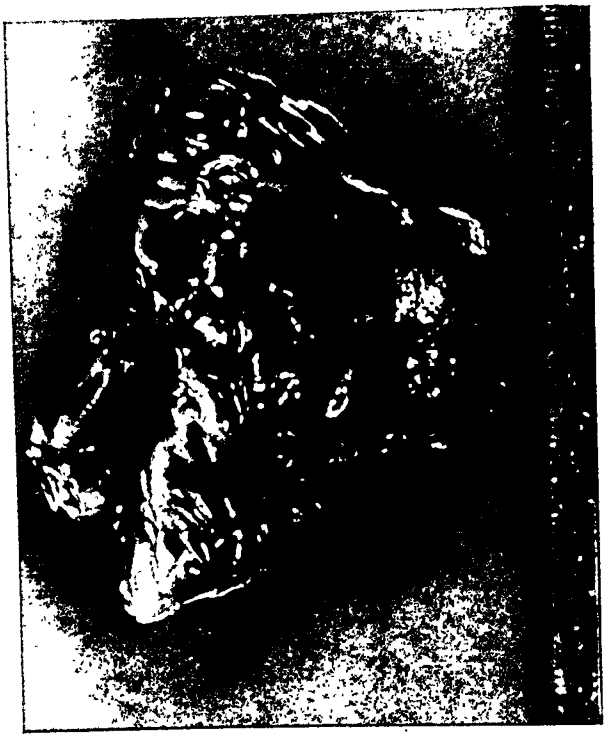

Fig. 5.—Jejunum opened showing ulceration of fibroma with drop of blood coming from ulceration.

During an examination for a bleeding episode one and one-half years prior to this admission, a completely asymptomatic adenocarcinoma of the right kidney had been discovered on pyelography. This was removed uneventfully, with no subsequent symptoms. The history and systemic review were otherwise noncontributory.

The patient was well developed and well nourished, but she appeared quite pale. Her blood pressure was 112/68 mm. Hg, pulse 116 per minute, and respiratory rate 20 per minute. Minimal epigastric tenderness was noted by one examiner, as well as a positive tourniquet test when blood was drawn for typing. The physical examination was otherwise negative. The tentative diagnosis was bleeding peptic ulcer, with blood dyscrasia and metastatic adenocarcinoma to be ruled out.

The hemoglobin level was 6.8 Gm. per 100 cc. on admission, and the white blood cell count was 12,500 per cubic millimeter, with a normal differential. The microhematocrit reading was 25%, urinalysis was negative, and stool examination was repeatedly positive for occult blood. The upper gastrointestinal x-ray series, chest x-ray, and bone survey were negative. Seven transfusions over an eight-day period maintained the hemoglobin level at only 6 to 8 Gm. per 100 cc., finally bringing it up to 12 Gm. prior to operation. This was despite intensive ulcer therapy.

Operation was carried out on Dec. 4, 1957, and revealed a polypoid lesion in the jejunum, 11 in. from the ligament of Treitz. This was removed by wedge resection with end-to-end anastomosis. There was no evidence of tumor in the left renal area. The pathological report was leiomyoma of the jejunum. The postoperative course was entirely satisfactory, the patient being discharged after eight days.

Summary and Conclusions

Benign tumors of the small intestine can no longer be considered rare, since the total reported cases exceed 1,400. They are being reported with more frequency, particularly as newer x-ray techniques for studies of the small intestine have been developed.

Although many cases are asymptomatic and are found incidentally at operation or at autopsy, of all the documented cases, 70% were found at operation and a considerable percentage of these were symptomatic. Less than 8% of all patients operated on have been given diagnoses before surgery. This figure could be raised to nearly 50% by proper x-ray examination, and a few series have approached this figure.

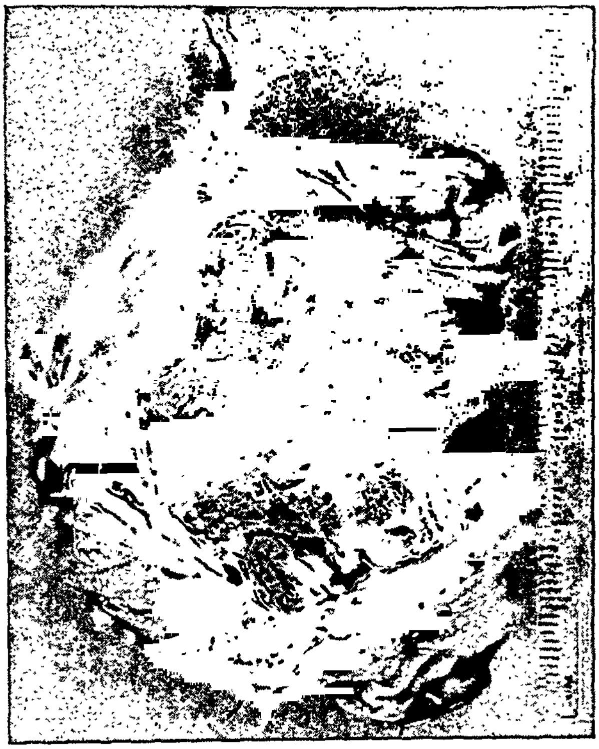

Fig. 6.—Tumor sectioned to show fibrous character.

Most series show benign tumors to be less frequent than malignant, and they are also less apt to be symptomatic. The etiology is essentially unknown. The sex incidence is equal, and the majority of these tumors occur in patients between 30 and 60 years of age. One-half of all cases occur in the ileum, the duodenum being the rarest location.

Most benign tumors are polypoid, and the most common presenting symptom is obstruction. The majority of these obstructions are due to intussusception. In fact, the majority of cases of intussusception in adults are due to benign tumors of the small intestine. The second most common symptom is bleeding. Diagnosis in the case of massive bleeding is usually late, and the mortality is fairly high. Tumor of the small intestine should be considered in patients with upper gastrointestinal bleeding without hematemesis in whom the upper gastrointestinal x-rays are negative.

Treatment is surgical and is directed at the simplest method of removal, usually either enterotomy with simple excision or resection with end-to-end anastomosis. The results have been relatively good, although the over-all mortality is about 20%; there has been a marked decline in recent years.

In the three cases of benign jejunal tumors reported here, all patients were admitted with massive upper intestinal bleeding. One of them also had obstruction due to intussusception. Preoperative diagnosis in all cases was probable bleeding duodenal ulcer, although the presence of tumor was considered. Upper gastrointestinal x-rays in all cases were either negative or misleading, including a series of the small intestine in one instance. Excellent results followed resection in all our cases.

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AGED INFIRM RESIDENTS IN A CUSTODIAL INSTITUTION

TWO-YEAR MEDICAL AND SOCIAL STUDY

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The feasibility of a method of disability evaluation in aged infirm people was tested in a group of 115 residents of a custodial institution. They were observed over a period of two years, at the end of which time about half of those remaining in the institution were over 75 years of age. A continuous process of rehabilitation was shown to be necessary in these patients. It involves restoration, reactivation, and maintenance and is especially important in those who have been admitted from a hospital or are temporarily hospitalized during their residency. There is a tendency for them to continue at the low level at which they were functioning when discharged from the hospital. This is a major problem in a domiciliary institution. Its solution requires the cooperation of the family and the community. Periodic disability evaluation and assessment of the patient's resources are essential. During the period of the study seven residents were discharged from the county home to their community.

A selected group of 115 aged, infirm individuals were thoroughly screened in order to serve as the basis for a determination of the feasibility of a method of disability evaluation. This system was subsequently called the "Physical Profile (PULSES)" and has been described previously.[1] The objective was to develop a method for expressing the ability of an aged, infirm individual to perform routine physical activities within the limitations imposed by various physical disorders.

This study deals with a two-year review of the same group of patients, with use of similar medical and social techniques to evaluate their problems. All the individuals were residents of a county home, living under similar conditions, with careful control of their medical problems by the same personnel throughout the entire two-year period of observation. In addition, an adjacent county hospital was available for all acute surgical and medical care, and complete diagnostic and laboratory facilities were available. Complete records were kept on all patients, and the hospital charts were thoroughly reviewed. Reexaminations were carried out at periodic intervals, averaging not more than three months, and a new physical profile was assigned each patient to indicate his functional capabilities. The residents received comprehensive medical care, including physical rehabilitation services provided by the county hospital. Social service was provided by the staff of the home on an on-going basis.

During the two-year period there were 36 deaths, constituting 31% of the entire group. It is rather significant to note that there was only one postoperative death. Pulmonary complications accounted for one-third of the deaths; these included five cases of pulmonary emboli, none of which were postoperative. The major cause of death was cardiac in 10 patients (coronary occlusion in 8 and congestive heart failure in 2), pulmonary in 12 (bronchopneumonia 6, pulmonary embolus 5, and pulmonary hemorrhage 1), cerebral in 4 (cerebrovascular accident 3 and parietal meningioma 1), urinary tract infections in 5, gastrointestinal in 2 (intestinal obstruction 1 and perforated duodenal ulcer 1), and miscellaneous in 3. All but one of the patients died in the hospital; the terminal illness was less than 10 days in 66% of the cases.

Of the 79 individuals surviving the two-year period, 25, or 32%, required varying periods of hospitalization, with a total of 38 admissions. The medical causes for hospitalization included pulmonary infection 7, urinary tract infection 5, control of diabetes 4, and cerebrovascular accident 2. The surgical causes included trophic and stasis ulcer 6, amputation of the lower extremity 3, cataract 3, disease of the urinary tract 3, hip fracture 1, carcinoma of the esophagus 1, and miscellaneous 3. There was only one hip fracture in the entire group. Peripheral vascular disorders involving the lower extremities were a frequent cause for hospitalization. One patient with an inoperable carcinoma of the esophagus was the only patient hospitalized for a malignancy. The relatively low

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incidence of urinary tract surgery is explained by the fact that several male residents had a prostatic resection prior to their admission to the home.

The Resident

At the end of the two-year period, 71.4% of the residents were at a level of complete independence, either in a wheel chair or on an ambulatory basis. In addition, four individuals were transferred to noninfirmary sections of the home where they did not require any supervision in their care. Seven were discharged from the county home to the community, and five were subsequently revisited in their own homes. In each instance, it was obvious that the individual had improved in the home situation, and there were no requests for readmission to the county home. This substantiates observations previously made in another study,[2] where it was established that once the pattern of rehabilitation had been set it continued within the home, guided by the proper motivation of interested relatives. Undoubtedly, this could be accomplished in more instances if community attitudes were changed.

Marital Status of Residents in a Custodial Institution

	Male	Female	Total
Single	30	12	42
Widowed	25	29	54
Separated	5	4	9
Divorced	4	..	4
Married	4	2	6
Total	68	47	115

Despite all efforts, nine residents underwent progressive physical deterioration ultimately necessitating complete nursing care. These patients constitute what may be termed the hard-core nursing problem in any domiciliary institution for the aging. Four individuals were transferred to psychiatric institutions when their mental problems could not be controlled in the domiciliary setting. However, there were many other marginal patients who were able to make the necessary adjustment to the sheltered setting in the county home. Some of these residents had previously been certified for transfer to psychiatric facilities.

Of the 115 residents in this survey, 56 (49%) were admitted from hospitals and nursing homes; 33 of these came directly from the adjacent county hospital, 16 from voluntary hospitals, and 7 from nursing homes. Fifty-nine residents (51%) came directly from the community; 16 were from a room and board facility, 27 from their own home or apartment, and 10 from a home with relatives; 6 were transient males.

The marital status of this group is illustrated in the table. Ninety-four per cent of the group had been living in a single status. Seventy-four persons were self-sufficient financially, through personal savings, odd jobs, and various types of pensions and other remuneration such as social security. Public assistance was rendered to 41, or 36%, as their sole method of community maintenance. A study of the occupational histories revealed that the majority of these individuals came from the unskilled, nontechnical categories. There were no professional people in this group. However, there were five white collar workers.

The age distribution of those individuals still remaining in the county home at the end of the two-year period is as follows: age 45 to 49, 1 person; age 50 to 54, 3; age 55 to 59, 6; age 60 to 64, 5; age 65 to 69, 13; age 70 to 74, 3; age 75 to 79, 7; age 80 to 84, 13; age 85 to 89, 6; age 90 to 94, 4; and age 95 to 99, 2. Almost 51% are over 75 years of age.

During the two-year period of observation, there were transitions in the physical profile of many residents. They reflected changes in their physical status without necessarily any alteration in their medical diagnoses. Some individuals improved, others became worse, and many maintained their physical and mental status. In addition, others underwent deterioration after acute illness and subsequently required assistance in returning to their previous functional level. This was termed reactivation in contrast to physical restoration. The latter term was applied to the rehabilitation of those residents who had incurred disabilities primarily involving the neuromuscular or musculoskeletal systems, such as a stroke or a fractured hip. However, it should be noted that the rehabilitation process was, of necessity, an on-going program, for it was equally important to maintain many of these patients at the maximum functional level which had been achieved, either in their reactivation or in their physical restoration program. This previously described program[2] has been termed a maintenance type of physical rehabilitation; it has been described also by Costello and Tanaka.[3] At the end of the two-year period of observation, 54% of the remaining patients were considered to be on such a maintenance program.

Comparison of the various components of the physical profile again substantiates the original findings, namely, a preponderance of disabilities involving the lower extremities which underwent the greatest deterioration. This is illustrated in the figure. In contrast, the upper extremities showed very little change during this same period. As anticipated, the incidence of incontinence increased, but there were only four totally incontinent patients at the end of the two-year period among those who had survived.

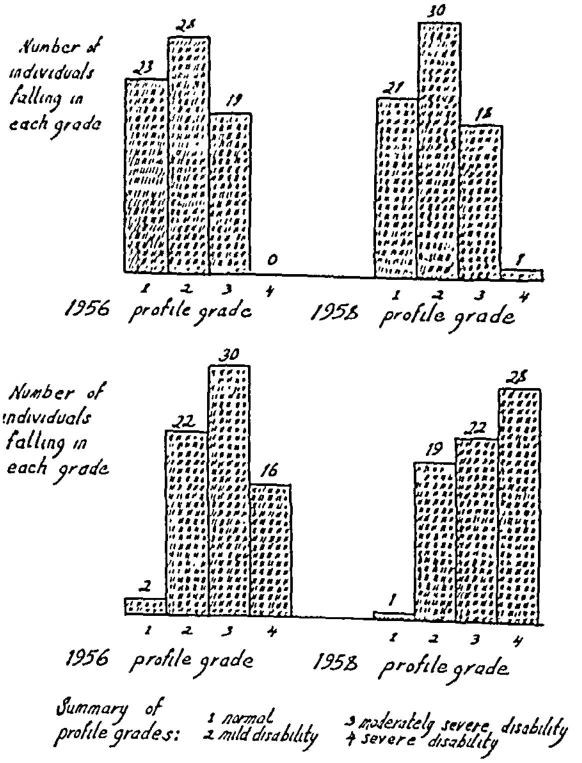
Rehabilitation Program

The introduction of a physical rehabilitation program in a county home more than three years ago has gradually crystallized a new concept in custodial care. The aging resident frequently becomes chronically ill and infirm. Rather than requiring pure domiciliary care on an ambulatory basis, these people need adequate medical and social services to meet their daily on-going needs as they arise. There is an increasing tendency to consider these domiciliary institutions as points of no return, not only from the medical but from the sociological perspective as well. While these individuals are, of necessity, housed in an institution devoted to the care of this type of patient, it does not necessarily follow that they should not be exposed to the same general medical and rehabilitation concepts which are carried out in the community. A bedridden individual in a domiciliary institution constitutes the major problem in nursing care. It is therefore necessary to be on the alert for comparatively minor defects which could ultimately lead to increasing this problem.

Originally, the physical profile was developed as a guide for those concerned with the care of the domiciliary patient. It enables them to estimate roughly the physical and mental abilities of any person. Periodic reevaluation enables one to determine exactly what is happening to the person. The physical rehabilitation program is geared to the specific needs of the individual at any one particular time. It has been recognized that the patient may undergo physical and mental deterioration without any changes from the diagnostic point of view. Teaching an individual to walk to the bathroom can influence his dietary habits as well as his mental attitude and behavior in the area where he is domiciled. Most elderly people have a tendency to take to a chair or to other sedentary activities, and an organized program of activity is vital for maintaining their physical capabilities. Contractures in the lower extremities, particularly the hips and knees, are very prone to develop from protracted sitting. A mild contracture may make the difference between an ambulatory and wheel chair existence. Periodic reevaluation of these individuals, with an estimate of their capabilities as reflected in the physical profile, immediately calls attention to these changes and initiates the proper corrective measures.

As previously noted, many individuals were hospitalized for intercurrent infections or other medical and surgical complications, and it was necessary to reactivate them after these illnesses. This is one of the major problems in a domiciliary institution. There is a tendency for them to continue at the level at which they were functioning at the time of discharge from the hospital. This is particularly true of individuals who are transferred from voluntary hospitals where the facilities are limited for any type of activation program. They are transferred soon after the termination of the acute phase of the illness, but this does not imply maximum physical restoration.

From the social point of view, it is equally important to change the concept of the domiciliary institution. It has been extremely difficult to work with relatives in making adequate plans for possible discharge of those who have improved during the course of their institutional care. In those instances where there is any hope of further rehabilitation, it is necessary to maintain an on-going casework service in order to make the family understand that there exists the possibility of improvement in the resident in a custodial institution, with the ultimate goal of return to the community.



Comparison of upper (*above*) and lower (*below*) extremity profile gradings in 70 patients in 1956 and 1958.

However, it should be recognized that in any domiciliary institution there are a given number of patients who require complete, permanent nursing care. By making more individuals self-sufficient, it should not be assumed that one can reduce the cost of domiciliary care. It does enable a greater allocation of manpower to those persons who require complete care. This recognizes the fact that no domiciliary institution can easily recruit and maintain a complete staff at all times.

Summary and Conclusions

In a two-year study of 115 aged, infirm individuals, a system of disability classification, termed the "Physical Profile," served as an effective index for recording the physical and mental status of the patients. The rehabilitation of a domiciliary patient is a continuous process involving restoration, reactivation, and maintenance, with transitions from one phase to another to meet the changing needs of the individual. Various disabilities affecting the lower extremities constituted the major factor in loss of rehabilitation potential. The terminal illness, averaging less than 10 days in 66% of the deaths, was the major cause for hospitalization in this domiciliary group. The changing population of domiciliary institutions requires a careful screening and follow-up program for recognition of the convalescent or deteriorating aged, infirm individual who can benefit from an organized activity program.

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CHRONIC GASTRITIS

HISTOLOGICAL CRITERIA FOR MANAGEMENT AND MEDICAL TREATMENT WITH A MUCOSAL ANESTHETIC IN ALUMINUM HYDROXIDE

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Gastroscopy with multiple biopsies shows that in severe chronic gastritis the mucosal pattern is distorted by irregular distribution of the gastric glands, increased numbers of mucus-secreting cells, and inflammatory infiltration of the stroma. The pattern of symptoms (pain-food-pain cycle) and failure to respond to antacids also distinguish chronic gastritis from the typical peptic ulcer. Ninety-two patients with chronic gastritis were treated with bed rest, sedatives, gastric suction, meals planned not to exceed the patient's critical volume, and a combination of aluminum hydroxide gel with oxethazaine hydrochloride, a topical anesthetic. While the severe forms of chronic gastritis were refractory to this treatment, the moderate and mild forms proved amenable, and the combination of antacid and anesthetic afforded relief from pain for periods up to six hours after each dose. Medication was continued for six days to 18 months without evidence of significant side-effects.

In planning an adequate program for treatment of chronic gastritis, a satisfactory method is urgently needed with which to obtain objective evidence for correlation with the clinical symptoms of gastric inflammation. The use of gastroscopy[1] and multiple biopsies has enabled formation of a definitive plan for management of the problem. Criteria for evaluation of the histological picture are suggested in table 1. This is especially useful in the large number of dyspeptic patients for whom the roentgenogram is negative.

Traditional treatment of chronic gastritis has paralleled that of peptic ulcer, but the pain pattern is usually quite different. In ulcer the characteristic sequence is pain-food-relief; in gastritis, pain-food-pain. Upper abdominal distress and bloating after meals are the commonest complaints. Nausea and vomiting become more prominent as illness is prolonged. Weight loss may reach 40 to 80 lb. (18.1 to 36.3 kg.) in the severe form. Achlorhydria is noted in 10 to 15% of cases. The standard ulcer regimen —diet, antacids, and anticholinergics—usually fails to relieve symptoms of gastritis.

Classification of Gastric Histology

Normal.—Normal human gastric mucosa presents a compact and regular glandular pattern. The glands contain one to three parietal cells and the remainder are chief cells in a symmetrical placement around the circumference. Mucus-secreting cells are generally insignificant. The stroma is

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sparse because of the compact glandular structure. The muscularis mucosae is thin and uniform without evidence of scarring or inflammatory infiltrate. The vessels throughout the sections are generally inconspicuous (see figure, *A*).

TABLE 1.—*Criteria for Histological Evaluation of the Gastric Biopsy*

- General architecture
  - Mucosa normal or showing inflammatory lesions (gastritis)
  - Tumor
- Epithelium and glands
  - Normal
  - Abnormal
    - Individual cell character and inflammatory change
    - Absence of acid cells
    - Intestinalization—excessive production of mucus
    - Cystic change in glands
    - Evidence of injury and repair
    - Mitotic activity, tendency toward reversal of nucleus-cytoplasm ratio
- *Stroma*
  - Interstitial infiltrate
    - Extent—cells per high-power field
    - Character of infiltrating cells
    - Lymphoid aggregates with and without germinal centers
- Muscularis mucosae
  - Normal
  - Abnormal
    - Cellular infiltrate
    - Edema
    - Hypertrophy
    - Evidence of injury and repair—scarring, glandular elements
- Congestion of vessels

Mild.—In mild chronic gastritis the glandular pattern is not significantly altered. Small numbers of inflammatory cells (lymphocytes and plasma cells) are haphazardly distributed throughout the interstitial tissue, with occasional slight displacement of the glands. The muscularis mucosae generally is uninvolved by this process (see figure, *B*).

Moderate.—In moderate chronic gastritis the mucosal pattern is moderately distorted with irregular distribution of the individual glands. Early intestinalization of the surface epithelium is present. The interstitial infiltrate is increased and more uniform in distribution, with formation of discrete lymphoid follicles. Some disruption of the muscularis mucosae is seen secondary to extension of the inflammatory process from the mucosa (see figure, *C*).

Severe.—In severe chronic gastritis there is considerable distortion of the mucosal pattern owing to compression and asymmetrical distribution of the glands. Increased numbers of mucus-secreting cells indicate a definite conversion to colonic-type epithelium. The stroma contains a heavy inflammatory infiltrate with many lymphoid follicles, some with active germinal centers. Fragmentation of the muscularis mucosae is seen secondary to inflammation and fibrosis (see figure, *D*).

Present evidence [2] suggests that mesenchymal cells may be unicellular endocrines which produce histamine, heparin, hyaluronic acid, and serotonin. In time of stress these may react as part of the mesenchymal system. This system includes fibroblasts, mast cells, and basophils. The chronic inflammatory infiltrate which seems to be a prominent part of the picture in gastritis may also participate in the functioning of the mesenchymal system.

The mechanism underlying the frequently described feeling of fulness and bloating may possibly involve the presence of gastric stretch receptors in the muscularis mucosae and their vagal afferent fibers, as suggested by the experiments of Paintal [3] in cats and of Towbin [4] in dogs. Towbin's experiments suggested that the reflex pathway lies in the vagus. The reflex arc consists of the gastric stretch receptor, vagal fibers, and the midbrain.

It is conceivable that in the presence of chronic inflammation of the stomach, such gastric receptors will respond to a smaller than normal volume of fluids and food, with immediate satiation of thirst and hunger. On increase of the water or food intake above this level (critical volume), gastric distress develops:

Inhibition of Histamine-Stimulated Gastric Acid

Many investigators have studied the role of the gastric antrum in controlling gastric secretion.[5] It is believed that in dogs in which the Heidenhain pouch has been established, the antrum, if exposed to or distended by food with a pH of 3.0 or above, releases gastrin to stimulate secretion in the pouch. In the presence of greater acidity, no secretion is stimulated. In the fasting state, the Heidenhain pouch yields no free gastric acid.[6]

TABLE 2.—*Diagnosis in Ninety-two Patients Examined and Treated for Inflammatory Gastric Lesions*

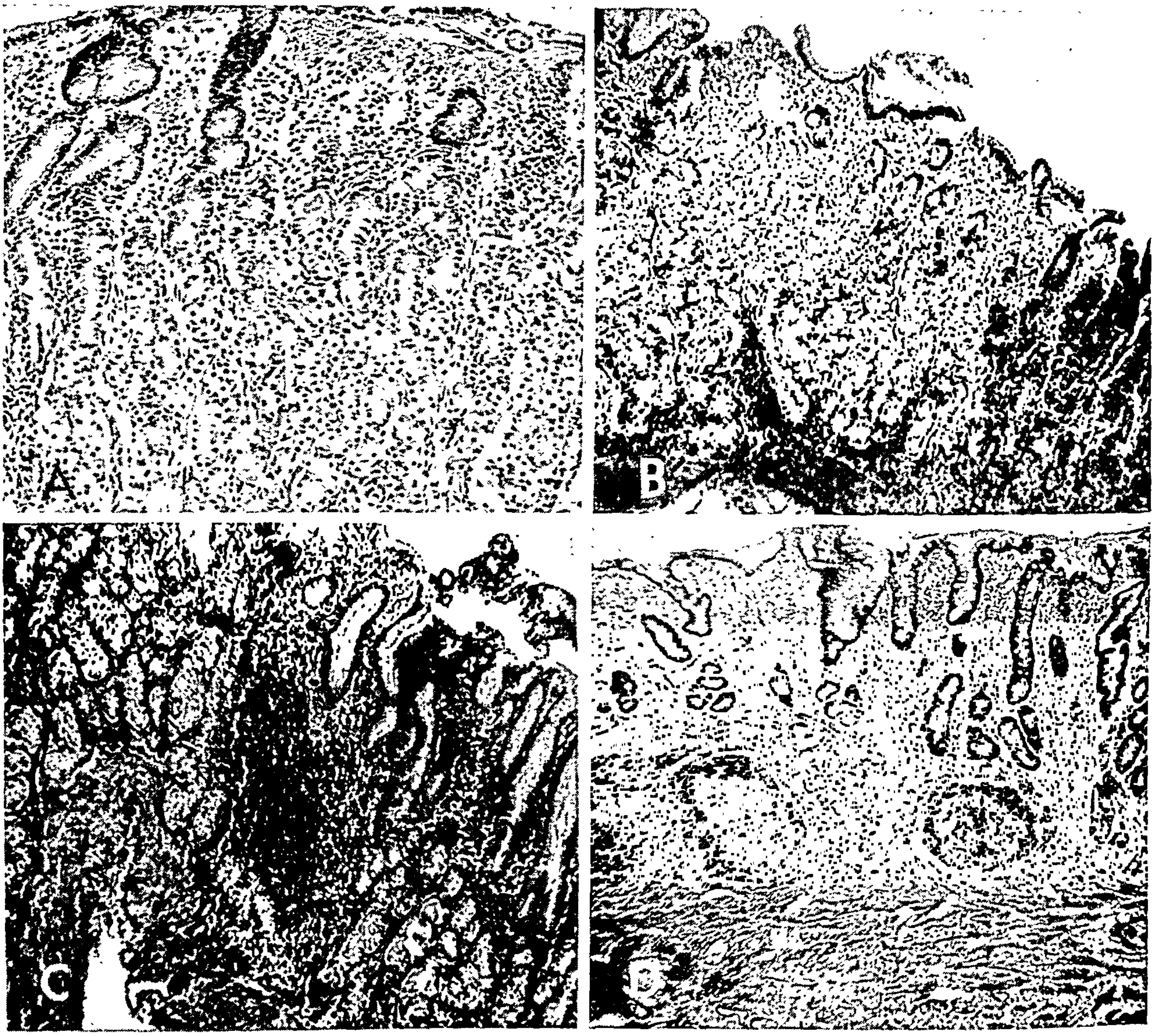
Diagnosis	No. of Patients
Chronic gastritis without associated disease	18
Chronic gastritis associated with	
Gastric atrophy—pernicious anemia	1
Postoperative gastritis	1
Mucosal gastric ulcer	8
Deep chronic gastric ulcer	1
Duodenal ulcer	12
Hodgkin's disease (after definitive surgery)	1
Hodgkin's disease (before definitive surgery)	1
Colon irritability	18
Chronic ulcerative colitis	7
Cancer of colon	1
Portal cirrhosis	2
Hiatal hernia	3
Migraine	4
Chronic relapsing pancreatitis	5
Postoperative cholecystectomy syndrome	1
Chronic cholecystitis	1
Narcotic addiction	1
Glomerulonephritis	1
Myocardial infarction, congestive heart failure, arteriosclerotic heart disease	3
Hypertension	1
Severe deforming arthritis	1
	92

In other experimental studies, application of a topical anesthetic to gastric mucosa blocked histamine-stimulated secretion of gastric acid [7] and prevented contraction of guinea pig ileum.[8]

Clinical Investigation.—A series of 92 patients, 13 to 81 years old, who had chronic gastritis, were examined and treated throughout a two-year study (table 2). Clinical evaluation included repeated history-taking, physical examinations, laboratory studies, and gastrointestinal roentgenograms. To determine whether the lesions were diffuse or patchy, gastric biopsies were routinely taken from three sites—antrum, midstomach, and fundus—in 39 cases, during gastroscopy with the Benedict gastroscope. The material was fixed in 10% formalin, stained with hematoxylin and eosin, and examined by several pathologists in various hospitals in and around Boston. At the same time the gastric aspirate was submitted for Papanicolaou stain and cell block.

Treatment.—Bed rest is essential for all such patients, especially when exhaustion is present. For recurrent episodes of nausea and vomiting, constant gastric suction for 24 to 48 hours affords the speediest relief. After gastric suction the patient is usually pain-free and well prepared for roentgenologic examination of the gallbladder and gastrointestinal tract, laboratory studies, gastroscopy, and surgical exploration if required.

The critical volume of food should be evaluated for each individual and should not be exceeded. Fast days, with bed rest, once or twice a week, help to prevent or diminish the severity of recurrent episodes of pain. Sedatives promote sleep.



Chronic gastritis. *A*, normal gastric mucosa from midstomach proximal to antrum. *B*, mild gastritis: sparse inflammatory infiltrate into interstitial tissue without significant alteration of glands. *C*, moderate gastritis: some disruption of glandular pattern and formation of lymphoid follicle. *D*, severe gastritis: extensive inflammatory infiltrate with lymphoid follicles containing active germinal follicles, intestinalization of glands, and fragmentationof muscularis mucosae.

Medication.—In the majority of the series, doses of 1 tablespoonful of aluminum hydroxide gel three times daily previously had afforded some relief for periods of about two weeks. Since clinical trials of a 0.2% concentration of a compound with local anesthetic action, oxethazaine hydrochloride [N,N-bis-(N-methyl-N-phenyl-t-butylacetamido) beta hydroxyethylamine hydrochloride][7] in aluminum gel, had shown therapeutic efficacy and safety, this combination was used for these patients. One teaspoonful (5 cc.) of the 0.2% solution of oxethazaine hydrochloride in aluminum hydroxide gel (which provides 10 mg. of the topical anesthetic) was administered before meals three times daily. Medication was continued for 6 days to 18 months.

Results.—Ninety-six per cent of the patients obtained complete relief of substernal pain or upper abdominal distress lasting two to six hours after each dose. Four per cent had only partial relief.

The 18 patients who had chronic gastritis with irritability of the colon had not improved on bland diet, anticholinergics, and aluminum hydroxide gel alone. The oxethazaine-aluminum hydroxide preparation permitted earlier use of water, fresh fruits, and fresh vegetables, followed by rapid improvement in bowel function.

The upper abdominal pain experienced by seven patients who had moderately severe chronic ulcerative colitis associated with chronic gastritis was relieved by the medication and the irritability of the gastrocolic reflex was considerably diminished.

The intervals between recurrences were longer and the episodes were milder in severity and more easily controlled. The medication did not mask symptoms of malignant processes in the stomach or colon. No significant side-effects developed.

Comment

Subjective symptoms of an intensity disproportionate to the degree of histological change demonstrated by gastric biopsy were best managed with psychotherapeutic measures. Thus recurrent attacks were reduced and unnecessary operation avoided.

The mild and moderate stages of chronic gastritis appear clinically to be reversible. The severe stage corresponds to the refractory form which fails to show significant improvement under medical management.

The cell block, made from aspirate at the time of gastroscopy, contributed little, although frequently it did contain recognizable gastric mucosa. When ulcer is present in the stomach or duodenum, and the biopsy specimens show normal gastric mucosa or mild or moderate gastritis, the ulcer usually heals under the medical regimen described. If, however, the biopsy specimens exhibit severe chronic gastritis, associated ulcers thus far have been refractory to medical management and appear to be best treated by operation.

Summary

Without biopsy, there is no confirmation of the presence, frequency, type, or extent of gastric pathology. The gastroscopic picture is poorly correlated with the histology of the gastric biopsy. Based on the histological criteria, three well-defined stages of chronic gastritis (mild, moderate, and severe) are recognizable. The severe stage of chronic gastritis appears to be irreversible and corresponds to the clinically refractory type. Mild or moderate chronic gastritis, with or without associated peptic ulcer, usually heals under the medical regimen proposed: gastric suction, physical rest, fast days, smaller meals, and a mucosal anesthetic administered orally in aluminum hydroxide. Peptic ulcer associated with gastritis in the severe form usually does not heal under medical management and is best treated by operation.

469 Beacon St. (Dr. Deutsch).

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CLINICAL NOTES

AGENESIS OF THE BLADDER

James F. Glenn, M.D., Durham, N. C.

Complete absence, or agenesis, of the urinary bladder is an extremely rare developmental anomaly, encountered in only 1 of nearly 600,000 patients seen at Duke Hospital in the past 28 years. Less than 10 instances of agenesis of the bladder are noted in the literature, and these are primarily of academic interest, noted at autopsy.[1] Campbell reports an incidence of seven cases in nearly 20,000 autopsies, most of which showed multiple developmental anomalies.[2] Some recorded cases of agenesis actually represent hypoplasia, contracture, or extreme degrees of exstrophy. This report deals with an instance of agenesis of the urinary bladder with several interesting clinical features.

Report of a Case

A 3½-year-old American Indian girl was admitted to the pediatric service of Duke Hospital in August, 1958, for evaluation of congenital heart disease. Complete cardiologic evaluation, including cardiac catheterization, disclosed a small interventricular septal defect, and it was felt that surgery was not indicated.

At the time of this admission, members of the pediatric staff noted that the patient had continuous urinary dribbling. Urologic consultation was requested. The patient's external genitalia were grossly normal, but careful observation revealed four pin-point openings in the urethrovaginal septum from which urine could be seen issuing.

The patient was discharged and readmitted to the urology service one month later. Information obtained from the parents indicated that no attempt had been made to toilet-train the child, and the parents had noted that the child's diapers remained wet at all times. The patient had 11 siblings, all of whom were said to be without urologic difficulties. With the exception of the cardiac murmur and the continuous leakage of urine the general examination disclosed nothing remarkable. Laboratory data included a normal hemoglobin value and white blood cell count. Blood urea nitrogen level was 36 mg. per 100 cc. Intravenous urograms revealed poor concentration of mediums with bilateral hydronephrosis and hydroureter and reduplication of the upper collecting system on the left.

With the patient under anesthesia a patulous urethral opening could be sounded to 1.5 cm. The vagina was sounded to 4 cm. The four orifices in the urethrovaginal septum were probed, and two of them were found to be fistulas communicating with the other two openings. Two 4 F. ureteral catheters were introduced into the orifices and retrograde pyelograms were taken, revealing bilateral hydroureter and hydronephrosis with reduplication of the left renal pelvis and upper ureter. A 16 F. McCarthy cystoscope was passed into the vagina, which appeared to be grossly normal. A normal cervix was visualized. Cystoscopy revealed the urethra to be a blind pouch about 1.5 cm. in length. There was no evidence of a vesical neck, nor could a trigone be visualized. The mucosa was thin and hypoplastic in appearance. Foley catheters were positioned in the vagina and urethra and were then alternately filled with a radiopaque medium. A urethrogram and a vaginogram were taken. The vaginogram is shown in figure 1. The urethral pouch measured approximately 1.5 by 1.5 cm. when completely distended. Figure 2 shows the artist's concept of the urologic findings.

It was evident that some form of urinary diversion was necessary since no bladder existed and since there was stenosis of the external ureteral orifices with consequent obstruction. Abdominal exploration and ileal loop urinary diversion were performed. After anastomosis of both ureters to an isolated segment of ileum, brought out in the right lower quadrant, approximately 6 cm. of the remaining lower portions of both ureters was excised. The pelvis was carefully inspected and a bicornate uterus noted. The patient's ovarian tubes and ovaries appeared normal. No bladder could be palpated. A normal appendix and a Meckel's diverticulum were removed.

The patient's postoperative course was uneventful. The blood urea nitrogen level became elevated transiently in the postoperative period. Urograms at discharge from hospital showed some resolution of the bilateral hydronephrosis. Adequate urinary collection was achieved through the use of an ileostomy bag. No further urinary leakage through the perineum occurred.

Developmental Anatomy

The development of the genitourinary system is a complex process. The bladder proper arises from entodermal cloaca, while the trigone and ureters arise from mesoderm (mesonephric ducts). The trigone and ureters are hence of Wolffian origin, but the vagina is derived from the Müllerian duct. It has been pointed out that since the vestibule and the ureters have a common origin in the Wolffian body it is not uncommon to find anomalous ureteral openings in the vestibule.[3]

Ectopic ureteral openings are frequently encountered, often associated with supernumerary ureters.[4] Most frequently, ectopia of the ureteral orifice occurs in the urethra or near the external meatus.[1] Extreme cases of ureteral ectopia are recorded,[5] and persistent cloaca has been noted in females.[6]

The most common developmental anomaly of the bladder is exstrophy, and this fortunately occurs in only about 1 in 50,000 births.[7] Agenesis of the urinary bladder is of still less frequent occurrence. Hypoplasia, or dwarf bladder, is also an extreme rarity. Congenital absence of the vagina, on the other hand, is a more frequent anomaly.[8] In dealing with these congenital genitourinary anomalies, emphasis must be placed on a thorough knowledge of the embryology, development, and anatomy of the genitourinary tract.[9]

From the Urologic Division, Department of Surgery, Duke University Medical Center.

Comment

This case of agenesis of the urinary bladder represents a rare urologic anomaly, but it also emphasizes certain aspects of pediatric urology which are of interest to the pediatrician, the urologist, and the family physician alike. It is interesting that this child exhibited multiple congenital anomalies in addition to agenesis of the bladder: a ventricular septal defect was demonstrated and the patient was also found to have double left kidney, a bicornate uterus, and a Meckel's diverticulum. In addition, it should be noted that this child's parents were of a North Carolina American Indian community which is notorious for its high incidence of familial intermarriage.

The most important aspect of this case is the feature of urinary incontinence. It has been previously stated that ectopic ureters are a frequent occurrence, and it is well known that urinary incontinence in children is often of surgical significance.[10] Lanman stated that 50% of children dying from pyelonephritis could be shown to have urologic obstructive lesions which would have been amenable to surgical therapy. Thorough medical evaluation of urinary incontinence is therefore mandatory in all cases.

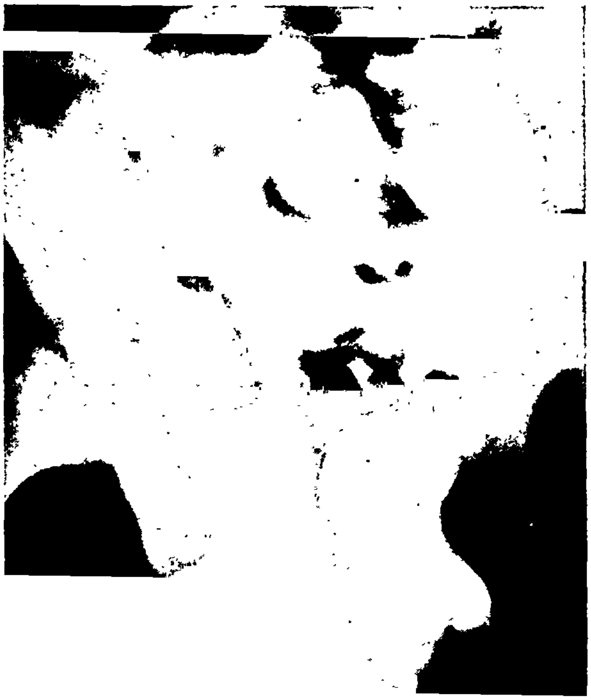

Fig. 1.—Vaginogram of patient. Tip of second catheter remaining in urethra is seen.

The first step in evaluation of urinary incontinence is recognition of the condition. Thorough education of parents is required if they are to observe the urologic habits of their children. Many infants are never observed in the act of voiding, and a surprising number of mothers are unaware of the intervals between diaper changes. A diaper which is continuously wet despite frequent changes is naturally one of the first signs of urinary incontinence.

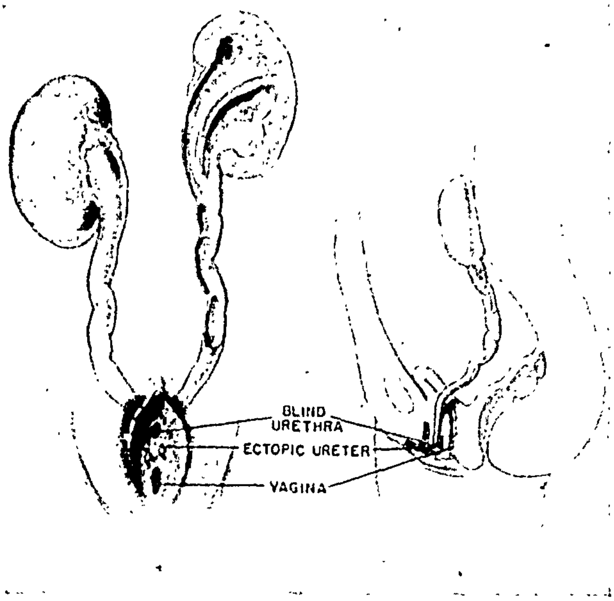

Fig. 2.—Composite drawing showing blind urethra, ectopic *orifices, bilateral hydroureteronephrosis,* and left double kidney.

Urologic evaluation should not be delayed. Ectopic ureteral orifices are usually surrounded by tissue producing obstruction and leading to prolonged urinary infection with pyelonephritis and renal damage. Other cases of urinary incontinence are equally serious, including bladder neck obstruction due to contracted vesical orifice or congenital urethral valves with resultant overflow incontinence. Congenital urinary fistulas with or without communication with the gastrointestinal tract also demand early surgical correction.

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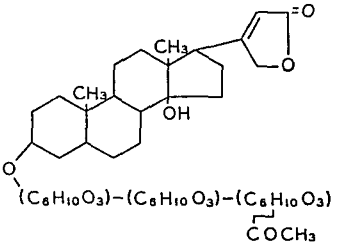
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based upon available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Acetyldigitoxin (Acylanid).—The alpha acetyl ester of digitoxin.—The structural formula of acetyldigitoxin may be represented as follows:



Actions and Uses.—Acetyldigitoxin, introduced in 1954, is a crystalline cardiac glycoside which is derived from lanatoside-A (a naturally occurring glycoside of Digitalis lanata) by chemically controlled, enzymatic removal of a glucose molecule. Clinically, the drug produces the therapeutic and toxic effects of digitalis and related principles. Acetyldigitoxin is characterized by a relatively rapid onset and a short duration of action as compared with digitoxin. Typical digitalis effects become discernible within two to four hours after oral administration. Because the drug is dissipated more rapidly than digitoxin, its effect is more quickly reversible; signs of intoxication disappear within one to three days after discontinuing treatment. Approximately 66% of an orally administered dose is absorbed from the gastrointestinal tract.

Acetyldigitoxin is used in the same manner as other cardiac glycosides for the treatment of congestive heart failure and/or auricular fibrillation and paroxysmal tachycardia. The drug has a high rate of fixation to serum albumin and is, therefore, well suited for maintenance treatment in chronic heart failure. Its bradycardic effect is pronounced in patients with auricular fibrillation who have a rapid heart rate. (See the general statement on digitalis and related principles in New and Nonofficial Drugs.)

Although acetyldigitoxin has shown a slightly more favorable therapeutic ratio in some studies, its toxic potentialities are the same as with other digitalis preparations. As with all other cardiac glycosides, constant supervision is imperative to avoid the adverse effects of overdigitalization. Gastrointestinal symptoms, which may be expected in approximately 20% of patients despite the most careful adjustment of dosage, are indicative of excessive dosage. Such effects usually precede cardiac arrhythmias and are readily reversible upon reduction in dosage or discontinuance of medication.

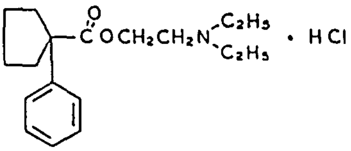
Dosage.—Acetyldigitoxin is administered orally for digitalization and maintenance. Since the drug is a pure glycoside, which is chemically well defined and stable, it is standardized gravimetrically rather than by biological assay. Dosage must be carefully adjusted according to the response of the individual patient and the appearance of toxic manifestations.

For rapid digitalization, 1.6 to 2.0 mg., with an average of 1.8 mg., is given within 24 hours, either as a single dose or in three or four divided doses. Some investigators have employed as much as 3.0 mg. in one day for initial digitalization, but this dose appears to be excessive from the standpoint of toxicity. For slower digitalization, daily amounts ranging from 0.6 to 1.4 mg., with an average of 1.0 mg., may be given for two to six days. Alternatively, the drug may be given in doses of 0.2 mg. three or four times daily until the therapeutic effect is achieved. The average maintenance dose of acetyldigitoxin is 0.15 mg. per day, with a range of 0.1 to 0.2 mg.

Preparations: tablets 0.1 mg. and 0.2 mg.

Sandoz Pharmaceuticals, Division of Sandoz, Inc., cooperated by furnishing scientific data to aid in the evaluation of acetyldigitoxin.

Caramiphen Hydrochloride (Panparnit).—2-Diethylaminoethyl 1-phenylcyclopentanecarboxylate hydrochloride.—The structural formula of caramiphen hydrochloride may be represented as follows:



Actions and Uses.—Caramiphen hydrochloride, introduced in 1949, is a synthetic antispasmodic agent which is used in the medical management of paralysis agitans (Parkinson's disease). It may be classified pharmacologically as an atropine-like drug. However, it has much weaker mydriatic and antisecretory effects than do the belladonna alkaloids while, at the same time, exerting a potent spasmolytic effect on smooth muscle. Caramiphen also relieves spasticity of voluntary muscle, an action believed due to peripheral cholinergic blockade plus central inhibition on cerebral motor centers.

Caramiphen is generally considered to be better suited for so-called postencephalitic Parkinsonism than for the "arteriosclerotic" or "idiopathic" types of the disease. The drug apparently has little effect on tremor but, in favorable cases, may afford some relief from rigidity. This relief is by no means complete; therapy is usually considered beneficial if muscle spasm is relieved by about 25%. As with other anti-Parkinsonian agents, there is no reliable criterion on which to predict responsiveness to caramiphen. In general, however, patients who respond well to the belladonna group of drugs will also show a favorable response to caramiphen. Although caramiphen appears to serve a useful purpose for the symptomatic treatment of some patients with paralysis agitans, it should be borne in mind that the long-term management of this disease with any therapeutic agent is unsatisfactory.

Giddiness and weakness occur frequently during the course of therapy with caramiphen. Other less frequent side-effects are chiefly atropine-like and include dryness of the mouth, blurring of vision, dizziness, faintness, and hypotension. Owing to its anticholinergic classification, caramiphen should be used cautiously, if at all, in patients with glaucoma, prostatic hypertrophy, urinary retention, or marked vegetative nervous system dysfunction.

Dosage.—Caramiphen hydrochloride is administered orally. Dosage must be highly individualized according to therapeutic response and appearance of side-effects. Initial dosage should be low, and the increase gradual. Changes from other anti-Parkinsonian medication should also be gradual, without abrupt stoppage of the previously used drug. Individual doses of 12.5 mg. may be given five times on the first day, with daily increments of about 50 mg. in the total daily dose until disagreeable side-effects begin to outweigh the beneficial effects. Maintenance doses generally range from 90 to 600 mg. a day, given in divided doses at intervals of two to three hours, throughout the day.

Preparations: tablets 12.5 mg. and 50 mg.

Geigy Pharmaceuticals, Division of Geigy Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of caramiphen hydrochloride.

Safflower Oil (Saff).—An oily liquid extracted from the seeds of the safflower, Carthamus tinctorius. Safflower oil contains 74.5% linoleic acid and 6.6% saturated fatty acids.

Actions and Uses.—Safflower oil is a natural substance rich in linoleic acid, an essential unsaturated fatty acid. When given in sufficient quantities to subjects with hypercholesteremia, certain unsaturated fatty acids (including those in corn oil and cottonseed oil) have been reported to lower serum cholesterol levels. This effect is variable and is not readily discernible in subjects with normal or near normal cholesterol levels. Safflower oil does not lower serum cholesterol levels to any appreciable extent unless it is substituted for saturated fatty acids already in the diet. For maximal lowering effects, it is necessary to achieve a certain ratio of food fats; this ratio should be approximately one part saturated fatty acid to three parts unsaturated fatty acids. This means that, for an appreciable effect, large amounts of unsaturated fatty acids such as those in safflower oil must be given while the intake of ordinary dietary fat is drastically reduced.

Safflower oil was introduced in 1957 and is proposed for clinical use in patients with hypercholesteremia with a family history of heart disease, in patients who have suffered myocardial infarction, and in those displaying evidence of coronary insufficiency. The rationale for such use stems from the statistical relationship that is commonly supposed to exist between elevated blood cholesterol levels and the frequency of atherosclerosis and its clinical complications. The fact that there is a significant statistical relationship between two variables does not prove that one causes the other. Nevertheless, it seems reasonable to postulate that sustained reduction in blood cholesterol levels, for which safflower oil is proposed, may be desirable. It remains to be shown, however, that safflower oil or any other cholesterol level-lowering agent has any effect, good or bad, in terms of the over-all physical status of the patient. Its clinical use must therefore be considered experimental.

In contemplating the use of safflower oil, it should be borne in mind that the proposed daily dose provides about 450 calories. If taken without a corresponding reduction in regular dietary calorie intake, weight gain may be expected. This is undesirable, since obesity in itself is commonly associated with elevated blood cholesterol levels. In fact, hypercholesteremia may often be improved simply by a program of weight reduction. For these reasons, special care should be given to the administration of safflower oil to obese patients.

Except for a slight tendency to produce diarrhea, safflower oil has been notably free of side-effects. Like other fats, it is a cholecystagogue and should be used cautiously in patients suffering from gallbladder disease.

Dosage.—Safflower oil is administered orally. The proposed daily dose is approximately 75 cc. of a 65% emulsion given in divided doses. To have any effect, therapy with safflower oil must be accompanied by a simultaneous reduction in the intake of animal fats and hydrogenated vegetable oils.

Preparations: emulsion (oral) 65%.

Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of safflower oil.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The Council has authorized publication of the following report.

PHILIP L. WHITE, SC.D., *Secretary.*

AWARD OF RESEARCH FELLOWSHIPS IN CLINICAL NUTRITION

Ten fellowships for research in clinical nutrition have been awarded by the Nutrition Foundation, Inc., and the Council on Foods and Nutrition. They have been given in honor of Dr. Virgil P. Syndenstricker, recipient of the 1958 Joseph Goldberger award in clinical nutrition. A fellowship is granted to a medical student to permit him to carry on research in some phase of clinical nutrition during the nonacademic portion of the school year. Each grant consists of $600. Application is made by a senior investigator, and the fellowship is administered by him. The Council was impressed with the interest shown in these fellowships and had a difficult time selecting 10 from the many meritorious applications submitted.

This fellowship program is a part of the joint effort of the Nutrition Foundation, Inc., and the Council on Foods and Nutrition to stimulate staff members and students of schools of medicine to take a more active interest in the science of nutrition as an integral part of medical practice.

The 1959 fellowships have been awarded for the following research:

1. Niacin and niacin-containing cofactors in hepatic lymph. Senior investigator, L. S. Dietrich, Ph.D., department of biochemistry, University of Miami.
2. The possible biosynthesis of vitamins A and D in fish. Senior investigator, James H. Jones, Ph.D., department of biochemistry, University of Pennsylvania.
3. The effects of iron stores and growth on iron absorption. Senior investigator, Thomas C. Chalmers, M.D., department of medicine, Harvard University.
4. Vitamin supplementation and the excretion of urinary oxalate. Senior investigator, Hans H. Zinsser, M.D., department of urology, Columbia University College of Physicians and Surgeons.
5. Cholesterol and carbohydrate metabolism. Senior investigator, W. H. Sebrell Jr., M.D.; student, Kenneth J. Berkes Jr., Institute of Nutrition Sciences, Columbia University School of Public Health and Administrative Medicine.
6. Studies on the rate of hydrolysis (in vivo and in vitro) of vitamin A esters. Senior investigator, Edward G. High, Ph.D., biochemistry department, Meharry Medical College.
7. The determination of body density of infants and children and the effect of diet on body composition. Senior investigator, Samuel J. Fomon, M.D., department of pediatrics, State University of Iowa.
8. An enzymatic and metabolic study of specific amino acids and the effect of certain nutritional conditions. Senior investigator, Alton Meister, M.D., department of biochemistry, Tufts University.
9. Protein and amino acid requirements of rats following experimental injury. Senior investigator, Otto W. Neuhaus, Ph.D., department of physiological chemistry, Wayne State University.
10. The relationship of lipemia clearing to coronary artery disease. Senior investigator, John F. Mueller, M.D.; student, Robert Poe, department of internal medicine, University of Cincinnati.

MEDICINE AT WORK

- Danger—Garment Bags!
- Health of Workers
- A Shoestring Clinic
- Rural Health Session
- What Is Psychotherapy?
- Rehabilitation Directory

Credit at the Hospital

The use of credit cards has become so widespread that at least one confident card holder tried to use his recently to pay a traffic fine. The fact that he failed indicates only that traffic courts are included in the diminishing minority that still insist on hard cash payment. Even hospitals, it appears, are taking the cue.

In Savannah, Ga., the 55-bed Telfair Hospital has instituted a credit card system of its own. Theirs is actually an improvement on the standard system since it not only establishes an immediate credit standing, but also relieves the patient or his family of lengthy recital of social history, formerly required for admission.

Here is how it works:

Every person with a previous acceptable credit experience at the hospital is mailed a "Master Social Information Sheet." When the information is returned, a credit card is issued for each member of his family. At the time of hospitalization, the patient need only present this card to the admitting clerk.

Upon discharge, he is free to leave the hospital without business office clearance. A bill for all charges is sent at the end of the month.

Card requests from persons without past credit experience at the hospital follow the same procedure except that a full credit statement is obtained and the application is checked through the local credit bureau.

Telfair Hospital believes the new plan not only greatly facilitates admissions and discharges but builds good will at the same time.

Left, children risk death by suffocation when they toy with plastic material. *Right,* Dr. Paul B. Jarrett, who recognized widespread hazard after four children died in Phoenix.

How One Physician Warned a Nation

Medicine and the Press—A Case of Joint Effort to Sound an Alarm

Milton Golin

The stories his colleagues were telling to Dr. Paul B. Jarrett of Phoenix carried an ominously familiar ring. Four children had died in recent weeks—suffocation while playing. What were they playing with? The other physicians told him: Plastic garment bags—why do you ask?

Because he did ask, thousands of physicians and patients across the land now are alerted to another of the many dangers which threaten the lives of children in our growingly complex society. This is what happened after Dr. Jarrett became curious and got his answers:

He determined on further inquiry that a number of laundry and dry cleaning establishments in the Phoenix area—like places elsewhere in the United States—in recent months had been substituting thin plastic bags for the paper sacks previously used for finished garments. He also learned that some parents were tossing the plastic to their children as "toys" after removing the cleaned clothing. Often the happy youngster, quite naturally, would place the bag over his head. Dr. Jarrett is reasonably certain that is what happened to the four children who suffocated in his city. Listen to his version of what probably ensued:

"An electrostatic charge may have been generated by friction from handling. The youngster, in peering through this material, is apt to have it literally grab him through electrical attraction to his face. If this happens only the prompt intervention of an adult will prevent tragedy. This dangerous material won't tear when a child fights it. Dizziness, inability to think, spasms of muscles occur with more and more rapid breathing. Vomiting with inhalation of undigested food puts a finish to this terrible tragedy."

Time for Alert

Now came the time for alert. Dr. Jarrett, conferring with fellow officials of the Maricopa County Medical Society (he is chairman of the safety committee and is credited with bringing about installation of seat belts in all state highway patrol cars and in many private autos in Arizona), helped draft a warning bulletin. He sent a copy to the *Arizona*

Republic, a newspaper whose editorial staff immediately recognized a public service duty inherent in the news itself. A news photographer posed a picture of a boy hooded by a plastic bag, to further illustrate the hazard.

At the same time, the county medical society early this year notified Bernard J. Conley, Ph.D., secretary of the A. M. A. Committee on Toxicology, which for years has been sounding the alarm of child-poisoning dangers lurking in many innocent-appearing household chemicals (see box and also Medicine at Work, THE JOURNAL, Jan. 12, 1957). Dr. Conley, in turn, saw an urgent need to broadcast the notice.

Citing the situation in Phoenix and quoting from the newspaper report, he sent letters to Metropolitan health departments, poison control centers, and other interested groups and individuals in scattered parts of the country. The reaction was immediate. In New York City, the assistant health commissioner, Dr. Harold Jacobziner, helped prepare a technical notice entitled, "Infants Dying from Suffocation by Plastic Material," and it was distributed to all poison control centers, maternal and child staffs, and superintendents of hospitals in that metropolitan area. Chicago's health commissioner, Dr. Herman N. Bundesen, last month took similar action. And in other communities, large and small, the danger was made known, always with the cooperation of local newspapers. At last report, the National Safety Council was preparing to publish an alert in its *Home Safety Review*.

Lives Saved

There is no way of determining how many young lives will be saved because of one physician alerting many—and because of newsmen then carrying the word to millions. That young lives were and will be saved cannot be doubted, however—just as death is being averted in similarly immeasurable medicine-press efforts involving abandoned ice boxes, imported highball stirrers containing toxic beans, and poison-laden Christmas ornaments. In those efforts, too, starring public service roles have been played by individual physicians and individual newsmen, by medical societies at all levels, and by newspapers in all ranges of circulation.

Meanwhile, Dr. Jarrett, the Phoenix surgeon who helped sound the early alarm, feels it cannot be repeated too often. He says: "Such a horrible combination as a child playing with a venomous reptile would not result in death as quickly as suffocation by the plastic film which clings . . . with diabolical tenacity. These deaths are the result of carelessness. They could have been prevented. Through knowledge they will be prevented in the future."

Chairman of the A. M. A. Committee on Toxicology is Dr. Torald H. Sollmann of Cleveland Heights, Ohio. Other members are Drs. Harvey B. Haag of Richmond, Va.; Irvin Kerlan of Washington, D. C.; Jay M. Arena of Durham, N. C.; Arnold J. Lehman of Washington, D. C.; Edward Press of New York City; Mr. Justus C. Ward of Washington, D. C.; and Mr. Jerome Trichter of New York City. Bernard E. Conley, Ph.D., of Chicago, is Staff Secretary.

Stuff That Poisons

A recent compilation of newspaper clippings which cover the period of 1955 through 1958 shows that 707 persons died in the United States as the result of accidental poisoning. The A. M. A. Committee on Toxicology, which collects such news items, reports that poisoning from internal medications dominates the pattern of nonfatal injury. Next in frequency are cases due to insecticides and rodenticides—followed by household chemical agents, industrial and other solvents, and miscellaneous products such as cosmetics. Recently, the Committee secretary met with representatives of the National Safety Council and the National Association of Poison Control Centers to consider a public educational campaign on the prevention of accidental poisoning.

School Sports May Be Healthful, But They Are Not Health Education

The academic tendency to make health education a stepchild in the curriculum has become commonplace in some public schools.

It was with this in mind that the Joint Committee on Health Problems in Education recently called for a re-emphasis on health teaching. The Joint Committee—which unites the American Medical Association, and the National Education Association in common cause—did not ignore physical education; in fact another of the group's resolutions called attention to opportunities in this field. But members did take pains to point out that health courses deserve consideration on their own.

This resolution on health teaching, approved at the Joint Committee's meeting in Chicago last month, calls on educators to employ teachers qualified in this field, and to allow them adequate class time to develop a comprehensive program. Adequate class time is defined as one period a day for one year in both junior and senior high schools.

Other Joint Committee resolutions call for increased physician interest in the health and health education problems of schools, special attention to health challenges generated by the use of school buses, and control of the hazards inherent in the use of carbon tetrachloride in science classes.

Much of the Joint Committee's three-day session was spent in editing its publications, a common group activity. Less common was its appointment of a subcommittee to plan a 1961 ceremony to celebrate the Joint Committee's own birthday—its 50th.

When 64 Health Groups Foster The Well-Being of Workers

Medical societies, through meeting periodically in factories, can promote occupational medicine.

Consumers foot the bill when a company neglects employee health.

We are entering the atomic age without having solved all the health problems of the machine age.

Farming is more hazardous than any other single occupation.

Those sample points were brought out in Chicago last month for more than 500 representatives of government, labor, management, and medicine who attended a three-day forum sponsored by the National Health Council. The conference on "The Health of People Who Work," was under the chairmanship of Dr. James H. Sterner, medical director of the Eastman Kodak Company and a member of the A. M. A. Council on Industrial Health. The A. M. A. is one of 64 sponsoring agencies of the National Health Council. Following are selected quotes from participants in formal presentations, panel discussions and informal news conferences:

The medical society should foster education in the general area of occupational health during the undergraduate medical school years, since every physician will be called on to administer to the industrial worker at one time or another.

—Dr. Kieffer Davis, medical director,
Phillips Petroleum Company

The doctor needs from management adequate assistance and support to permit him to spend much more time in evaluating and improving the work environment than in sewing up fingers and dispensing pills.

—Dwight J. Thompson, executive vice-
president, Champion Paper and Fibre
Company

I would estimate that 90% of the health problems in industry are not occupationally-oriented, and that half of these are either emotional or have emotional overtones.

—Dr. David Goldstein, medical director,
New York Times

An industrial worker does not pick up his heart or his lungs or his body at the factory gate when he checks in. Nor does he leave them there when he checks out. Industrial health is tied up with home health.

—A. J. Hayes, president, International
Association of Machinists

Why is freedom of choice of physician important? Because it aligns the inherent drive of the doctor to succeed in his profession with the best interests of the patient and therefore the public. Common sense tells us that the physician's dedication to high professional standards will be reinforced by enlightened self-interest.

—E. J. Faulkner, president, Woodman
Accident and Life Company

Even with elaborate and early preparation, many who reach 65 become the lost generation when they are forced to retire. It is important to retire to something. To make a messenger boy out of a college president is to promote mental and physical deterioration.

—Dr. Frederick C. Swartz, chairman,
A. M. A. Committee on Aging

The vast number of organizations for health need to be seen not only in relation to their individual purposes, needs and values, but also as they relate to other health organizations and to the cultural, economic, political and scientific environment.

—Ruth B. Freeman, Ed. D., incoming
president, National Health Council

Dr. Freeman announced that next year's Forum will deal with "Health of Older People," under the chairmanship of Dr. Edward Bortz, former A. M. A. president and now a consultant to the Committee on Aging. That topic is as far-reaching, she noted, as this year's, which President Eisenhower described as follows in a telegram read at the opening Forum session on March 17:

"'The Health of the People Who Work' represents a challenge directly related to technologic progress in preventive health measures. It involves the well-being and productivity of almost 70 million workers. This is a challenge which can be met only by the combined efforts of management and labor, the health professions, government, private and voluntary health agencies, and civic and community groups."

Exams for Executives

Opinions that executives are more subject to unusual stresses and strains because of the positions they hold were critically evaluated at the most recent meeting of the A. M. A. Committee on Medical Care for Industrial Workers.

Members suggested that a 1957 A. M. A. policy statement on health examinations was just as applicable to executives as to other employees. They also felt that the examinations should be done locally to encourage continuity of care and follow-up. Committee members, citing observation and study, expressed the opinion that executives are not subject to any more stress and strain than other employees, but suggested that further exploration of such examinations, under adequate statistical control, might provide more reliable conclusions.

The Committee on Medical Care for Industrial Workers operates jointly under two Councils. Its report was discussed by the Council on Industrial Health last month and will be reviewed by the Council on Medical Service on May 2.

Industrial Health Posers

Immunization and Screening—Who, When, and for What?

What an occupational health program ought to do and how it ought to do it was suggested by the A. M. A. House of Delegates in a policy statement issued in 1957 (The Journal, July 6, 1957). But like all general documents, it dwelt on broad principles rather than specific judgments.

In an effort to shed light on some special problem areas that have become apparent, members of the A. M. A. Council on Industrial Health recently discussed proposed guide lines for industrial immunization programs and multiphasic screening examinations. The Council met in Cincinnati on Feb. 14 and 15 prior to the 19th annual Congress on Industrial Health.

In discussing a proposed guide for immunization, the Council pondered three major questions:

—Should an employer provide the protection for employees who, by reason of their occupation or job assignment, may be exposed to significant hazards against which immunization procedures are available?

—Should an employer provide these procedures in the face of an impending epidemic which threatens to disable so large a proportion of his employees as to interfere materially with operations, and against which immunization would not or could not be applied by community health resources in a short enough period of time to afford optimum protection?

—May an employer participate in community-wide immunization programs at the request of, and in cooperation with a local medical society and community health agencies?

On the matter of multiphasic screening examinations (relating to a battery of tests), especially those in which mobile laboratory units are used, committee members expressed the opinion that such screening, in selected instances, might be worthy of future trial if carefully conducted and confined to a relatively few, simple tests—such as urinalysis, hemoglobin level determination, differential blood cell count, and chest x-ray, according to the needs of the particular situation.

They felt that if such screening is related to the occupational environment, it should be considered to come within the scope, objectives, and functions of the occupational health programs, as set forth in the official A. M. A. statement. These same committee members also expressed the opinion that multiphasic screening should include provision for a follow-up program, that the tests should be performed by qualified personnel, and that the interpretation should be made by the individual's personal physician.

Members and staff of A. M. A. Council on Industrial Health meet in Cincinnati.

Rehabilitation Directory—New Instrument for the Physician

A patient recovering from severe illness or disability often needs more than continuing medical aid to resume his place in society. But how can physicians guide him to other agencies to meet his need for social service, vocational counseling, or job placement?

Feeling that this is an area in which state and county medical societies can be of help to their members, the A. M. A. Committee on Rehabilitation, meeting last month in New Orleans, approved a booklet that tells "how to do it." Called "Medicine's Back to Work Plan," the pamphlet is based on recommendations, made last December by the House of Delegates, which urges state associations to form committees on rehabilitation.

The purpose of these committees would be to review state-wide rehabilitation programs and to establish liaison with other groups interested in the problems of the disabled and handicapped. The House also recommended that state associations urge county societies to survey the rehabilitation facilities available in their areas.

Such surveys could be used, the booklet states, to develop informative rehabilitation services directories. Designed for the use of physicians and others interested in the challenges of rehabilitation, such directories should list hospitals, nursing homes, nursing agencies, rehabilitation centers, training schools, sheltered workshops, and social and family service agencies. A sample survey form and suggestions for the preparation of a local directory are included in the booklet, which states:

"More than two million disabled persons in the U. S. today could be restored to useful jobs—if shown proper guidance and care, taking into consideration the abilities they still have, and their physical limitations."

Keeping Them Healthy Down on the Farm

Hampered, but not defeated, by a late winter blizzard that boomed across the plains, nearly 600 rural residents from several Midwest states gathered in Wichita, Kan., last month for the 14th National Conference sponsored by the A. M. A. Council on Rural Health. They joined physicians, nurses, teachers, editors, extension workers, and dentists in discussions of such challenges as mental health, the cost of medical care, animal diseases that affect humans, and health education.

"How you feel about other people is one aspect of mental health," said Dr. Alonzo Peeke, a general practitioner from Volga, S. D. "It's also how you get along with yourself, and how you are able to meet the demands of life. It's far more than just the absence of mental illness."

Dr. Prescott W. Thompson cautioned his audience that facilities for the care of mental patients must be "hospitals" in every sense of the word. Dr. Thompson, who is director of outpatient service for the Menninger Clinic, said: "To the lay public, the mental hospital is the most visible evidence of what psychiatry is and what it has to offer. These hospitals must shed any resemblance to the old asylums with their gloomy exteriors, and their hopeless interiors."

Dr. Thompson believes that such rejuvenation is important for two reasons: The patient and his family must view the mental hospital as a treatment center—a place in which to get well; and a good mental hospital is the best means by which to recruit medical students and others into psychiatry and its related disciplines.

In discussing the cost of modern medical care, Dr. Conrad Barnes of Seneca, Kan., said: "Increases are mostly in the fields of drugs and hospitalization, and are certainly justifiable in the light of modern medical care." He noted that while modern drugs and hospital techniques may be expensive when compared with those of "grandfather's day," they actually constitute an economy in getting patients well faster and better. "Consider the reduction in communication time between major cities from days to seconds," Dr. Barnes said. "It was done only at a tremendous cost, but who would say the new service was not worth it; who would want to go back to the 'good old days'?"

Control of disease in animals, Dr. Martin P. Hines told the conferees, is an area in which enlightened rural groups cooperating with veterinarians, physicians, and public health workers have made dramatic progress. Dr. Hines is the chief of the Veterinary Public Health section of the North Carolina State Board of Health and a member of the Council's advisory committee. He noted that effective campaigns have been waged against Texas fever, bovine tuberculosis, and brucellosis. He warned, however, that other diseases have appeared to take their place. Leptospirosis is one; Q fever is another.

Despite the apparent success of modern agricultural methods, Dr. Hines pointed out that 10% of all farm animals died last year from diseases or parasites. "Mastitis alone," he said, "causes an annual 5% loss in milk production."

In addition, many animal diseases are secondarily transmissible to man. Such zoonoses now number more than one hundred. He said: "Among the difficulties contributing to the control of animal diseases are: the poor understanding of the ecology of man, animals, and birds; faulty diagnosis and reporting systems, and the fact that rural dwellers often feel they must live with many of these diseases."

Calling for a "temporary partnership between

One Woman's Opinion

"Take the tractor, boys, and pull old Doc Schneider out of that mudhole." The fact that her physician-husband was fresh out of internship made the terminology incongruous, but to Mrs. Kenneth Schneider of Brown County, Indiana, it also meant that she and her husband had been accepted by the rural community in which they had chosen to settle.

Some of the trials of their rural practice were told by Mrs. Schneider to those who attended last month's A. M. A. Conference on Rural Health, but the diminutive housewife and former nurse left her audience with no doubts about the country being a good place to live.

Mrs. Schneider told how she and her husband, both city reared, took the first plunge into practice in a town of 526 people in partnership with another married physician. Their first office (where she served as nurse) was in a makeshift space above an appliance store, and both couples lived in the same 50-year-old building. Today, they have a modern clinic, and Dr. and Mrs. Schneider live in a home built on an acre of rolling, wooded ground four blocks away. She says:

"Kenny does all those things many think a family doctor no longer does—performing minor surgery, setting fractures, prescribing medicine, delivering babies, making home calls, and acting as family confessor. The partnership assures us that patients will always be taken care of, and he still has time to spend with his family."

Romance sometimes became enmeshed with medicine in those first days. Mrs. Schneider recalled one time when she had gone with her husband on a night call, and he put his arm around her as they rode home in the moonlight. "Honey," he said as she waited expectantly, "did you notice that patient's hyperactive reflexes?"

Audience as well as program speakers air their views on multiple challenges of rural health at A. M. A.-sponsored National Conference in Wichita.

patient and physician during treatment," Dr. F. S. Crockett, chairman of the A. M. A. Council on Rural Health, said such an arrangement was vital to health. "The doctor examines, diagnoses, and prescribes," he said, "but it is the patient who must follow directions, and do what he can to get well and stay well."

Health Versus Patronage In Youngstown, Ohio

It took more than 14 years, but the Mahoning County Medical Society—with the help of dentists, druggists, veterinarians, and members of other health groups—finally has won its battle to get a full-time physician health commissioner for the 170,000 residents of Youngstown, Ohio. The story is another example of physicians working with others to solve a community problem (see Medicine At Work, THE JOURNAL, March 16, 1957).

The concerted effort that succeeded in amending the city's charter to call for a professional health officer began in early 1957 when the society's new president, Dr. Stephen Ondash, persuaded the group to take it on as a project. Even this was no simple matter since the society had tried repeatedly to persuade the city council to put such an amendment on the ballot for a referendum, and for 14 years the efforts had failed. The chief reason

Workshops Help Kansans Solve Their Own Health Problems

Participants at one session of the recent A. M. A. National Conference on Rural Health became citizens of an imaginary town called America. The purpose of the transformation was to show how community workshops are being used to help solve the health problems of many Kansas communities.

Such workshops are sponsored by the state medical association and its county societies and are guided by Dr. V. E. Wilson, assistant dean of the University of Kansas School of Medicine, and Mr. Oliver E. Ebel, executive secretary of the Kansas Medical Society. At the request of any Kansas community, they recruit a team of resource people—physicians, public health workers, educators, clergymen, engineers, and sociologists—to staff a meeting of the town's residents.

No attempt is made by the visitors to either identify the community's major health problems nor to volunteer possible remedies. Instead, the moderator asks individual residents to state their community's problems. In explaining the method to his Conference audience, Mr. Ebel said that such an approach usually elicits many difficulties the town is experiencing, and that the audience itself soon decides on those that are uppermost.

Having succeeded in identifying the problems, the moderator then asks members of the audience to suggest possible solutions. "Usually," Mr. Ebel told his listeners, "once the meeting has reached this stage, all it needs is guidance." Those who have attended as resource persons offer information only when asked and confine their remarks to relating the experiences of other communities with similar challenges.

Even those attending the Rural Health Conference, in their capacities as residents of the fictional town of America, found a good many things to be concerned about. The afternoon session generated considerable discussion about the length of time children must spend on school buses, the lack of physical examination requirements for school children, the travel required to see a dentist, and facilities for the aged.

In actual practice, Mr. Ebel said, these meetings may vary in length from one to three days and occasionally take some surprising turns. One gathering became so interested in the construction of hospital facilities that an expert in this field, missing from the resource panel on the first day, was alerted and arrived by plane in time for the second day's session. In another, enthusiastic citizens enticed members of the town's council into the hall for a full scale airing of a community sore point: garbage disposal.

was that the new position required a civil service rating, and politicians of both parties preferred to see it remain an appointive patronage plum.

A Public Health Committee headed by Dr. John J. McDonough first approached the city council with a request that the charter change be submitted to the voters. Expecting a refusal, it also went ahead with preparations for a widespread petitioning. The councilmen did refuse, and so the committee mounted a massive two-fold campaign—first to acquire the thousands of signatures necessary to force a referendum, and second to educate the citizens of Youngstown to the desirability of the charter revision.

Petitions were sent to every physician, dentist, chiropodist, and druggist in the city. Next went weekly letters reminding them of the importance of the effort. Their secretaries were spurred in their efforts to collect signatures by the offer of three cash prizes for the most successful, and members of the woman's auxiliary checked on the progress of their husband's petitions. When the time came to file, the committee found its petitions had 13,000 signatures, more than the required percentage to get the question on the ballot.

Then began the second stage of the campaign—to convince Youngstowners that they ought to vote for the charter amendment. With the aid of an advertising agency, a brochure was prepared explaining the value of a qualified health commissioner. A copy was mailed to every city residence, and other copies were displayed by doctors, dentists, pharmacists, veterinarians, and hotel keepers. Advertisements were placed in newspapers, and on radio and television. And above all, speeches were made. "I spoke publicly on the subject more than 30 times myself," said Dr. McDonough.

Voters saw the value of the amendment and passed it by a substantial majority last November.

For a time thereafter, it appeared that getting the charter revised might have been less of a task than finding a physician to fill the position it had created. The supply of doctors interested in public health did not begin to meet the demand.

Then, entirely unsolicited, Dr. Leonard A. Blum appeared. After 24 years of private practice in Niles, Ohio, he left to obtain a master's degree in public health. Having done so, he sought to return to his birthplace—Youngstown. On invitation, he met with the new board of health, and was hired.

Youngstown now has its first full-time, qualified health commissioner.

Shoestrings, Lions, and Doctors

Combining Salesmanship with Public Service in Quest for Better Health

Thanks to a handful of matchbooks and three scraggly shoelaces, medical service is available today in the little town of Ariton, Alabama (population 750). There's more to it, of course—such as people, perseverance, and pride in community. Also involved is an all but fantastic new twist on the old story about selling refrigerators to Eskimos.

The Ariton story began a half dozen years ago but is being reenacted in variation of theme throughout rural America—wherever and whenever communities and physicians need to be brought together (see Medicine at Work, The Journal, Sept. 29, 1956; Oct. 11, 1958; and Feb. 21, 1959). How did Ariton stop being a doctorless town? It was like this:

At a meeting one autumn evening, the local Lions Club decided it was high time to raise money to build a medical office. So they held a contest right then and there. Matchbooks were passed out and each member was asked to give an impromptu sales talk on the product or company imprinted on the cover. The three presentations adjudged best were delivered by E. L. Fralish, Kyser Wilson, and D. B. Richardson. Their prize was one shoelace apiece—with the mission of parlaying these stringy items into an initial campaign fund. One was sold for $1

Placement Straws in the Wind

What is the current status of doctor demand and supply? While not complete, some indication may be found in the following recent reports from the A. M. A. Physicians Placement Service:

—Industrial relations department representatives for defense project construction firms in Greenland, for the DEW (distant early warning) line in Canada, and for an electronics and missile firm in the U. S. are looking for medical directors at salaries of up to $25,000.

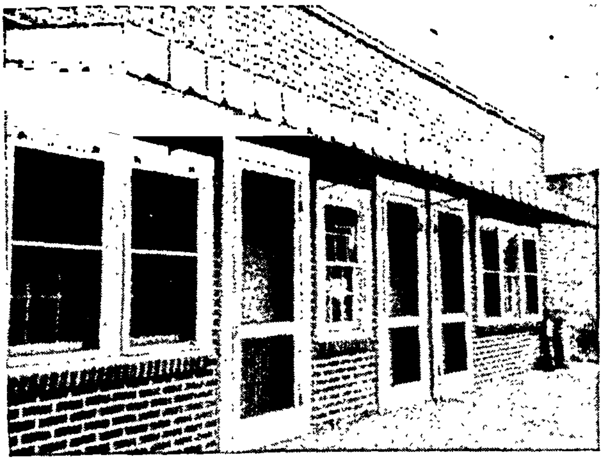
—Correspondence and observation in the past year indicate that a number of highly trained young surgeons are being forced into "quasi general practice," possibly because of a saturation of the specialty of surgery. The reason and extent of this condition cannot be determined for certain at this time; however, distribution studies, by specialty, are now under way.

—Liaison with the A. M. A. Council on Medical Education and Hospitals now is being refined so that medical schools and physicians with academic positions in mind may be brought together through the placement office, which functions under the Council on Medical Service.

and the money bought more laces, which then were sold for amounts ranging from a dime to a dollar. Within weeks, the "Shoestring Committee," with the help of merchants contributing other goods for sale, had a $300 kitty—plus a lot donated by the town for a medical office site.

Now came the supersalesmanship. Lions Club members decided to hold an auction unlike any other ever conducted anywhere. Townspeople would be invited to "bid" for the right to finance unseen assets of the unbuilt clinic building. This novel idea captured the imagination of Ariton—and it worked. Bidding $100, one citizen won over his neighbors for the "privilege" of giving and installing windows of the clinic. Another $100 offer entitled the bidder to dig necessary ditches for construction. A third $100 bid included the privilege of drawing up blueprints of the building. Other offers brought both money and materials for naming the clinic and installing a water fountain outside (see photo).

"It was the screwiest auction I ever attended," said one Lion, "but it sure caught on. Everybody, it seemed, was scrambling for the right to give money and be identified with the project in some special way. We soon had a seven-room clinic."



View of the medical office "built on a shoestring" in Ariton, Ala. Note, at lower right, water fountain, which was installed by a townsman who outbid his neighbors for the privilege of "sponsoring" it.

Lions Club members then began seeking a doctor to occupy it. One physician moved in after the A. M. A. Physicians Placement Service and the Medical Association of the State of Alabama went into action. But last year he moved away for health reasons and because the office was too far from his home. So again medical association help was sought—and last fall the townspeople turned out to welcome Dr. George M. Malouf, a graduate of the University of Vermont College of Medicine.

His may be the only medical practice in the nation that had its start, literally, on a shoestring.

When Lions Roar

Lions Clubs in many parts of the country have taken the initiative (along with Ariton; see story) to improve medical service. Because their activity has brought physicians to so many doctorless towns, closer liaison now is being established between Lions International and the A. M. A. Physicians Placement Service. Following are excerpts from letters to the placement office from local Lions Clubs:

"Our Lions Club has for its major project this year the procuring of a country doctor for our community. We have already procured a lot and we anticipate no trouble at all in financing the project as the public is very enthusiastic..." (Kentucky)

"Our Lions Club is greatly concerned about the medical services and facilities available to the people and industries of our community..." (Pennsylvania)

"Thanks to your placement service, we were able to secure a full time resident doctor, to take charge of our new Lions Club Medical Center..." (Indiana)

Replies to almost all such inquiries refer to the appropriate state medical society and include two A. M. A. booklets, "A Doctor in Your Community" and "Community Efforts Provide Medical Facilities." In addition, Miss Dorris Webb, the staff assistant at A. M. A. headquarters in Chicago, may suggest that the Lions Club obtain the free loan (through its local medical society from the A. M. A. film library) of a 28-minute color movie, "A Citizen Participates." It tells of a girl, ill in a Kansas town where there is no physician, and how members of a fraternal group go about bringing in a resident physician.

So far, reports Miss Webb, none of the Lions Clubs which showed the film have let out a peep about the fraternal group involved. It is Kiwanis, which helped make the movie in its own continuing efforts to improve medical service in communities.

Medical Electronics—The Fruitful Marriage

The patient is placed in position, the technician makes minor adjustments to his equipment, and then steps behind his shielding screen. . . .

When he sets his timing switch, the x-ray technician will be bringing into play the results of more than a half-century of cooperative effort between physicians and engineers that has resulted not only in highly refined radiological devices, but a host of other electronic marvels (see Medicine at Work, The Journal, March 21, 1959).

The debt that medicine owes to electronic engineering was cheerfully acknowledged this month by Dr. Gunnar Gundersen, A. M. A. President. Writing in *Electrical Engineering* on the occasion of the 75th anniversary of the American Institute of Electrical Engineers, he stated: "The progress of science and medicine over the last century has been hand-in-hand, each benefiting from the other's discoveries and developments, and ultimately helping mankind."

Dr. Gundersen wrote that modern x-ray units not only provide better and more discriminatory diagnostic help than earlier ones, but also decrease the amount of radiation the patient receives.

Some Views of Lawyers on The Physician as a Witness

Attorneys are as interested as physicians in improving interprofessional relations, judging by letters accompanying early returns to a questionnaire being used by the A. M. A. Law Division. In addition to filling out the four-page form, a number of lawyers spoke their minds on matters of mutual interest to both professions:

On Doctor-Lawyer Rapport—

"A doctor in general practice is usually not familiar with court trials and is somewhat handicapped in that he has to be taught how to handle himself in the trial of a case. . . . Some type of course should be taught at medical schools—if it is not already—to give some actual experience in testifying in a mock trial."

On Legal Theory—

"The essence of the American system of jurisprudence is the adversary character of the proceedings. A system under which—through vigorous contest—we seek to arrive at the truth. Lawyers accept this as a matter of course . . . yet the physician accepts the critical analysis of his testimony as a personal affront."

On Fees—

"With a large number of doctors, the attitude seems to be that they are doing an attorney a favor to appear in his case. From the defendant's standpoint, this is not true. Insurance companies are willing and do pay whatever reasonable fee is charged, and the doctors in turn should be willing to devote such time as is necessary to the proper presentation of the case."

On Differing Points of View—

"The physician's skills and training are oriented to minimizing the residual disability after the patient has had the maximum benefits of treatment. The plaintiff's attorney, in the role of advocate, must maximize the injury so that in our adversary system of justice the client's best possible case is made out. It is the duty of the defense to minimize the damage, so consequently the physician and the defense normally have common objectives."

Doctor Meets Attorney

Medicine and Law—Common Goals But Few Pat Answers to Problems

American jurisprudence is based on the adversary system—a partisan contest in which discovery of the truth is expected to result from the pleadings of opposing points of view. This same system was applied at a Washington conference last month when nearly 500 attorneys and physicians met to hear two-sided discussions of subjects in which medicine and the law have common interests.

Topic selection was varied, ranging from a sober evaluation of narcotics addiction to a humorous account of the presumed woes of a medical witness undergoing cross examination. The Washington session was the first of three similar regional meetings sponsored by the A. M. A. Law Division. Two more were scheduled for early this month in Cleveland and Salt Lake City.

Physicians who dread the thought of appearing as a medical witness through fear generated by tales of "ruinous" cross examination can relax, according to Irving Goldstein, professorial lecturer in trial technique of Northwestern University Law School. "I searched the entire country for documented examples of such technique to be included in a legal text," he said, "and I ended up with only five that were usable. A typically devastating question was 'Have you ever made a mistake, doctor?' "

Noting that law students are advised never to cross examine an expert in his own field, Goldstein said: "A physician who goes into court prepared to tell the truth, and who does not exaggerate his background and experience has nothing to fear." He warned, however, that the opposition will probably be well prepared on the medical subject in point and that the physician should review his own records, x-rays, and the medical literature prior to his appearance.

Impartial or Infallible?

Impartial medical testimony—that provided by an expert chosen by medical societies and appointed by the court—is another area in which the conference audience heard differing points of view.

G. C. A. Anderson, a former president of the Maryland State Bar Association, said impartial medical panels are the result of numerous cases in which conflicting medical testimony was presented by physicians "selected not for their medical qualifications or objectivity, but principally for their personality, manner of testifying, and jury appeal."

Metropolitan New York uses a rotating panel of expert witnesses available for call by the court to make pretrial examinations in matters of medical dispute. In Baltimore, a somewhat different plan is in effect. There the names of three experts are submitted to the parties in contest and they are asked to agree on one. If they cannot, the court makes the choice.

Drugs and Doctors

What is the physician's legal position if he prescribes narcotics for a patient who is an addict?

Federal law—and that of most states—limits the dispensing of narcotics by a physician to that done "in good faith and in the course of professional practice only." The catch comes in defining the phrase.

In 1922, the U. S. Supreme Court upheld an indictment alleging that a physician gave an addict prescriptions for 150 grains of heroin, 360 grains of morphine, and 210 grains of cocaine for use over a period of several days.

Then in 1925, the court reversed the conviction of a physician who had been charged under an indictment involving "four small tablets of morphine or cocaine."

In neither case was it alleged that the defendants failed to prescribe in the course of good professional practice.

The Joint A. M. A.-A. B. A. Narcotics Committee report of 1958 states: "There must be a new determination of the limits of good medical practice in the treatment of drug addiction, and an objective inquiry into the question whether existing enforcement policies, as well as existing laws, have unduly or improperly interfered with good medical practice in this area."

The trouble with all such plans, argued attorney Elwood S. Levy of Philadelphia, is that they "presuppose that medicine is an exact science." He said: "No fair-minded man can deny that in a substantial number of cases equally competent and equally honest physicians can and do disagree . . . It seems obvious that to label a doctor as impartial does not for a moment mean that he is right. . . . [Yet] by designating a medical witness as court appointed and impartial, the court has in effect cloaked him with the robe of infallibility and imports that his conclusions are more worthy of acceptance than those of his medical bretheren who have not been thus *distinguished*."

Rule of Sympathy

The extension of the legal doctrine of *res ipsa loquitur* ("the thing speaks for itself") was characterized by R. Crawford Morris of Cleveland as "the rule of sympathy." The fallacy in extending the application of this rule, he said, is that when a bad result follows an operation it is presumed that the reason for the bad result must be some negligence on the part of the surgeon.

Standard legal philosophy is that he who affirms must prove, but the extension of *res ipsa loquitur* in malpractice cases, Mr. Morris argued, "hurls the doctor into the lion's den." He said: "It makes the physician an insurer of perfect results, and deprives him of his right to have his conduct judged by other physicians fully aware of the facts he faced at the moment of his decision."

This view was disputed by Hugh Head Jr., an Atlanta attorney, who said the rule had been invoked in such obvious cases as that in which the surgeon operated on the wrong patient, where the patient was given 10 times the proper amount of anesthetic, and where an electric needle being used to remove skin growths had set fire to alcohol used as an antiseptic. The physician, in effect, he said, contracts to do his work well and is held liable only when he has broken his faith.

Both Morris and Head agreed that the reluctance of physicians to testify against their peers had made the courts tend to sympathize with plaintiffs. "Doctors must realize," Mr. Morris said, "that they cannot have their cake and eat it too. If they refuse to testify, courts will provide other means of redress."

Enforcement or Education

In the discussion of narcotic addiction, Alfred Tennyson, chief counsel for the U. S. Bureau of Narcotics, voiced the Bureau's long-held belief that strict enforcement of laws against the sale or purchase of narcotics for other than medical or scientific use was the best way to meet the problem. He said that experiments with big city drug clinics in the early 1920's had produced "no evidence of cures or reduction in illicit drug traffic." "Present methods," he said, have reduced the addict ratio in the general population from 1 in 400 in 1915 to 1 in 3,500 in 1958. He said he was dismayed to note that "some members of the medical profession" have sponsored a plan whereby government-operated clinics would supply the drug addict with narcotics while attempting to "persuade" him to undergo treatment and rehabilitation.

Tennyson's view was opposed by E. J. Dimock, Judge of the U. S. District Court in New York, who said: "If severe laws have had any effect on the [drug] traffic it has not shown up in our court." Judge Dimock was a member of the Joint Committee of the American Medical Association and the American Bar Association which undertook a study of the narcotic problem. He said the Committee found that not enough was known to support more than one or two conclusions. One recommendation was that the two parent organizations study further the outpatient experimental clinic plan.

Painless and safe withdrawal procedures are now in use at federal narcotic hospitals, he said, "but treatment that an addict gets there is of little help to him outside. We must learn how to help our fellow human beings to live without resorting to this destructive evasion in a world full of temptation and strains."

Judge Dimock advocated the prevention of first contact as the ideal solution to the narcotic problem. He said: "If none of us had taken that first glass of beer, we would never have had that how-long-has-this-been-going-on feeling."

Psychotherapy Is Medicine

The application of psychological methods in the treatment of illness is a medical function. Any physician may utilize the skills of others in his professional work, but he remains responsible, legally and morally, for the diagnosis and for the treatment of his patient.

When a resolution containing that statement was adopted jointly by special committees of three major professional groups nearly five years ago there already was evidence that a few nonphysicians were practicing medicine by engaging in psychotherapy. "Psychotherapy is a form of medical treatment and does not form the basis for a separate profession," the resolution went on to state, adding, however: "The medical profession fully endorses the appropriate utilization of the skills of psychologists, social workers and other professional personnel in contributing roles in settings directly supervised by physicians."

Now there are indications that more and more nonphysicians, not content with merely using psychological understanding in carrying out their professional functions, are attempting to diagnose and treat individuals by psychotherapy. The indications are so ominous, in fact, that the A. M. A. Council on Mental Health (which issued the 1954 joint resolution, along with the American Psychiatric Association and the American Psychoanalytic Association) discussed the problem at length during a meeting in Chicago several weeks ago.

Council members at their Feb. 21 meeting cited reports from colleagues as well as patients, in an attempt to clarify and reaffirm the resolution for the benefit of the public and the medical profession. Several of them expressed the opinion that it should be unlawful for a nonmedically trained psychologist to engage in the independent practice of psychotherapy, and unethical for a physician to refer patients to such an individual for treatment of nervous, mental or physical disorders.

At the same time, however, they applauded the functions of psychologists in medical settings, for psychodiagnostic testing, and for analysis and counselling in education, vocations, aptitudes and job placement. As one member summed up the discussion:

"It cannot be too strongly emphasized that the unavailability of a specialist in nervous and mental diseases is not sufficient justification for referring a patient to a nonmedical specialist for treatment. The physician should himself treat such a patient, and try to obtain or provide neuropsychiatric services locally in the future. To do otherwise only serves to compromise ethical practice and to lower the levels of medical care."

More Ammunition Against Alcoholism

New onslaughts upon alcoholism as a massive disease problem (see Medicine at Work, The Journal, July 19, 1958) were indicated at the recent meeting of the A. M. A. Council on Mental Health. Members expressed their approval of a suggestion that the Woman's Auxiliary consider alcoholism as a major project for attack in 1959. The Council also approved an outline which had been suggested by its Committee on Alcoholism as a guide for medical schools, which already are integrating alcoholism as a subject in prevailing curriculums.

Medical Students and Religion

How do tomorrow's physicians relate their religious attitudes to the study of medicine?

In an effort to find out, 208 students enrolled at the Southwestern Medical School in Dallas were asked recently to reply to a multiple-choice questionnaire. These are some sample findings:

"Do you consider yourself a religious person?" No, said 21 students, but 129 considered themselves to be at least "slightly religious."

"What about the study of medicine—is it making you more religious?" Ninety-one thought it was, 88 said it was not, and 21 thought it was making them "less religious."

In assessing the influence of religious considerations on their desire to enter the medical profession, 117 concluded there had been no such consideration, while 75 thought that there had. Nine out of 10 thought a religious nature would add to the effectiveness of a skilled medical practitioner.

Asked, "If an indicated medical procedure conflicted with your patient's religious beliefs, would you still urge the procedure?" 140 replied affirmatively, although when asked to comment, most said they would attempt to explain the necessity, and try to obtain consent.

Results of the survey were published last February in the *New Physician* by two medical students, James A. Hall, and Daniel Gruver. The authors reported that comments accompanying the returned questionnaires emphasized that these medical students, while generally considering themselves religious, disliked casting their beliefs in conventional forms. "My belief now boils down to the Superior Being, brotherhood, and compassion," one said. Only 27% said they believed in all the creeds and dogmas of their religion (see Medicine at Work, The Journal, April 13, 1957).

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DÉBRIDEMENT IS PARAMOUNT

GUEST EDITORIAL

John O. Goodsell, M.D.

COMPOUND fractures are emergencies. They require treatment promptly, for time is of the essence. Débridement is the keystone of the treatment.

The ideal treatment of the compound fracture devolves logically in a well-established chronological order. This begins with adequate first aid at the site of the accident, essentially splinting. Rapid, but safe, transportation to the place of definitive treatment ensues. Appropriate assessment of the victim's general well-being and measures for assuring its stability begin with first aid and are intensified on arrival of the patient in the emergency room. Local injuries are quickly but carefully evaluated. They are then treated and the all-important débridement performed in the case of compound fracture. Finally immobilization of the fracture is accomplished by whichever of many possible methods is best suited.

Why is débridement paramount? This can best be answered by observing that, while all infected wounds are at least unfortunate, infected fractures are catastrophes. No other single facet in the care of a compound fracture is so important in the prevention of infection as débridement. This principle has been irrevocably established for decades, but must frequently be "rediscovered."

Eaton [1] said in reference to débridement of compound fractures in World War II: "In spite of the experience gained in World War I, this lesson had to be learned all over again in the early part of this war." The literature of World War II is replete with references to the imperativeness of débridement. Few improvements in humanity result from war. It would be a pity if the costly lesson in proper débridement of compound fractures were not indelibly stamped in the consciousness of all who assume the treatment of trauma.

How débridement deters infection is made clear by Watson-Jones in his textbook "Fractures and Joint Injuries." [2] Débridement is the proper toilet of a contaminated wound, including removal of all tissue which is dead. Germs thrive in necrotic tissues which form a barrier between them and the body's natural defenses. Healthy vascular tissue can, given proper opportunity, deal successfully with germs.

Débridement should be performed as soon as the patient's condition will allow it. There is a "golden period" of six to eight hours from the time of injury when the wound may be considered merely contaminated rather than infected. After that the wound must be treated in anticipation that infection has supervened, and débridement is of progressively less benefit. By that time drainage and compresses may be more appropriate, alone or with débridement.

Some situations delay immediate débridement. Other injuries most often force temporary postponement. However usually such factors can be improved rapidly enough to stay within the "golden period." Shock from blood loss is the most common deterrent. It behooves the surgeon always to treat shock as vigorously as possible, first to preserve life and next to preserve the limb by early débridement. To save the patient's life may be heroic, but the surgeon's fatigue must be ignored until the fracture has also received its adequate treatment. The reward for such tenacity is great: avoidance of prolonged, sometimes seemingly endless, treatment of chronic osteomyelitis.

Some injuries, e. g., to the brain, lungs, liver, or spleen, may not permit débridement at the ideal time. All injuries to the head, chest, and abdomen do not automatically prevent proceeding, however. We must exert energy here also to distinguish the type present. Conceivably the presence of disease unrelated to the accident may interfere, e. g., diabetes or heart disease. Again we must distinguish when these things might reasonably be ignored or improved sufficiently to deal with the local injury.

Orthopedic surgeon, Saginaw, Mich.

The technique of proper débridement is dealt with in detail in various textbooks. The principle is excision and removal of all foreign material. This includes dead tissue, because it too is foreign. Skin removal should be minimal; usually a 2-or-3-mm. excision of the wound margin suffices. All dead fat, fascia, and muscle must go; left behind they can only liquefy and become a culture medium. Vessels and nerves should be identified and protected. Bone should not be removed unless totally detached from soft tissue. Copious irrigation with sodium chloride solution is invaluable in removing small bits of debris.

The use of internal fixation is somewhat controversial and in the opinions of some writers never applicable in compound fractures. Properly selected, nevertheless, internal metal appliances have been used in many such cases by many surgeons without significant complications.

To close or not to close is also a question. Opinions here vary from never to not over eight hours after injury, and even longer. Individualization is needed here too, with such things as amount and type of contamination, amount of skin remaining, and time after injury being important. There is fairly general agreement that if closure is elected, it should be of skin only, never fascia.

Antibiotics undoubtedly contribute to the success of treatment of compound fractures. It has been written again and again that the availability of these drugs does not alter fundamental surgical principles. Débridement of compound fractures is fundamental and cannot be eliminated nor even minimized by the use of antibiotics. A review of the World War II literature on compound fracture reveals a widespread wave of enthusiasm for placing sulfonamide powder in these wounds. One can scarcely doubt in the face of practically universal approbation that this helped. But this probably coincided with progressively better débridement. The ranks of the sulfonamide sprinklers are certainly smaller than they were.

To summarize, in the treatment of compound fractures débridement is paramount. It should be done as soon as possible, with special effort to do it less than eight hours after injury. Rapid treatment of shock and other delaying conditions should be carried out. The availability of antibiotics does not decrease the necessity of débridement, nor even the extent of débridement. Rapid, energetic treatment of a compound fracture is certainly rewarding.

Some of the ideas expressed herein are based on the observations of the late Dr. Sylvester J. O'Connor.

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1. Eaton, G. O.: Overseas Treatment of Compound Fractures of Long Bones, J. Bone & Joint Surg. 28:434-439 (July) 1946.
2. Watson-Jones, R.: Fractures and Joint Injuries, ed. 4, Baltimore, Williams & Wilkins Company, 1952, vol. 1.

MENTAL HEALTH WEEK, APRIL 26-MAY 2

The observation of Mental Health Week once again reminds us of one of the largest public health problems confronting the United States—mental illness. While the exact incidence of emotional disorders is not known, the rejection and discharge figures for psychiatric disorders in the armed forces in World War II, the current rates of hospitalization for the mentally ill and retarded, and the problems of alcoholism, narcotic addiction, juvenile delinquency, and broken marriages give some indication of how large the problem is. Physicians in general practice and internal medicine repeatedly have estimated that one-third to one-half of the patients they see have disorders which are primarily psychogenic or which are complicated by emotional factors.

The level of care of many patients in mental institutions is indeed low. It is reported that in some mental institutions with over 1,000 patients there is but one psychiatrist to provide treatment. The disproportion between the level of care given the hospitalized mentally ill patient and that given the patient hospitalized for a physical illness is one that medicine must strive to eliminate.

More research on the causes of mental and emotional illness and on more economical and more effective methods of treatment is urgently needed. What is known about prevention should be implemented as soon as possible and over as broad an area as possible. Physicians should be as capable of diagnosing mental illness as they are of treating uncomplicated medical or surgical illness. If the training of the physician does not achieve this, his training needs to be reexamined and changed. The training of the psychiatrist bears inspection also. He has tended to isolate himself from his medical colleagues and thereby to forego the advantages that collaboration and cooperation provide.

Now that great strides have been made in the prevention and treatment of infectious diseases, perhaps we can give more attention to mental illness and solve this serious problem, whether by biochemical, physiological, or psychosocial means.

JOURNAL INDEX

The index to volume 169 of The Journal will appear in the May 9, 1959, issue. Those who wish extra copies of the index may receive them, without charge, on request to the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

COUNCIL ON MEDICAL SERVICE

CHRONIC ILLNESS SERVICE CENTER OF SAN FRANCISCO

The Chronic Illness Service Center of San Francisco was established in October, 1950, as the result of two years of study and planning by a special subcommittee of the Social Planning Committee of the Community Chest. This subcommittee, after reviewing the problems of the chronically ill both nationally and in the San Francisco area, recommended a two-year demonstration program to test the feasibility and value of a central information-gathering, coordinating, and referral agency for the city's chronically ill. Originally supported by foundation funds and later by the United Community Fund in 1955 the Chronic Illness Service Center of San Francisco began operations directed toward the following objectives: (1) to promote the development of a coordinated community-wide program for adequate care of the chronically ill; (2) to assemble and make available information regarding the unmet needs and problems of chronic illness; (3) to assemble, study, and make available information on existing community facilities and resources for the chronically ill; (4) to stimulate public interest and understanding of the problems of chronic illness and its prevention and control; and (5) to assist organizations in planning facilities and programs for the chronically ill.

Organization and Operation

The original staff of the service center, which was housed rent-free in the Community Chest Building, consisted of a director and an office secretary. A medical social worker was added to the staff in August, 1952. The center functions under the guidance of a 21-man board of directors, who are familiar with the community and its resources and specifically concerned with the problems of chronic illness. Additional consultation and guidance is provided by a technical advisory committee, representing various professional groups with a knowledge of the key fields related to chronic illness.

The director's duties, in addition to over-all supervision of the administrative and program activities of the center, include liaison with the board of directors and the technical advisory committee, interpreting agency policies to the community and professional groups, consultation with individuals and groups planning resources for the chronically ill, preparing reports on the individual and community problems of long-term illness, and the planning of meetings and educational activities for specific groups.

The medical social worker is responsible for the day-to-day operation of the information, counseling, and referral service. Consultation with and referral of patients or other persons seeking suitable facilities for care is her continuing responsibility. She secures and maintains current information on the various facilities and resources for long-term care in the community and makes this information available to persons and organizations who need assistance in planning care for chronically ill or disabled patients. She also acts as a consultant to the operators of nursing homes and other long-term care facilities on administrative policies, needs of the long-term patient, and ways of improving care.

The office secretary, under direction, is responsible for the management of the office and the clerical-administrative details inherent in the center's operation, maintaining files, records and correspondence, and preparing monthly statistical reports. She also acts as receptionist and telephone operator.

The center occupies about 450 sq. ft. in the Community Chest Building and is divided into three offices. Inasmuch as the majority of referrals and information can be given by telephone and all office interviews are by appointment, the lack of space has not presented a serious problem as yet. Files maintained in the office include detailed data on proprietary nursing and boarding homes and other facilities and services currently operating in the community (this information is usually obtained by a questionnaire followed by a visit to the facility) and complete individual case records for all persons requesting services, which are divided according to new requests, recall cases, and persons seeking information not related to a specific patient.

Services to Patients

From the beginning, it was felt that emphasis should be placed on counseling, guidance, and referral services to individual patients and others seeking information and that in this way insight would be gained into the over-all planning, coordinating, and educational services needed in the community as a whole. In accordance with this policy, services were made easily available and individuals requesting help were accepted without being

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This is part of a series of articles, prepared by the Council on Medical Service, on chronic illness information centers in various parts of the United States.

obliged to undergo detailed investigative procedures. However, there was no emphasis on case-finding activities nor on publicity concerning the center's existence. An announcement letter was mailed to other agencies notifying them of the center's availability, and two articles describing the center were published in the San Francisco Medical Society Bulletin. No organized follow-up is made of patients to see whether the solution or the placement suggested has been completely satisfactory in each case.

TABLE 1.—*Persons Served in 1954, 1955, and 1956*

Year	Patients, No. New*	Recall†	Other, No.‡
1954	788	360	185
1955	1,087	641	276
1956	1,329	902	208

* Patients known to center for first time

† Patients who have received previous service from center.

‡ Requests for service not related to specific patient.

From its inception in October, 1950, to the end of 1956, the center provided services to 7,037 individual patients or other persons. During the calendar year 1955, 1,728 patients sought help at the center, an increase of 51% over 1954 (641 of these patients had received service previously from the center; the remainder were new referrals). Table 1 shows the number of services requested during the years 1954, 1955, and 1956, divided according to new and recall cases and requests not related to an individual patient. Table 2 shows the referral sources for both new and recall patients during the year 1956.

TABLE 2.—*Source of Requests for Patient Services*

Source	New Patients, No.		Recalls, No
Patients, relatives, and friends		721	709
Hospitals and welfare agencies			
Hospitals	327		
Other health agencies	47		
Family agencies	43		
Information services	17		
Relief agencies	5		
Miscellaneous	22		
Total		461	129
Other			
Physicians	54		
Nursing and boarding home operators	33		
Unions	12		
Press	9		
Nurses	7		
Employers	6		
Attorneys	5		
Trustees, guardians	4		
Clergy	4		
Insurance companies	3		
Landlords	3		
Fraternal & veterans organizations	3		
Professional associations	2		
Foundations	2		
Total		147	64
Grand total		1,329	902

Of the 1,329 new patients referred to the center in 1956, almost 60% were between the ages of 65 and 85. The average patient age has been steadily rising since the center's inception and was 71.6 years in 1956. Almost twice as many women as men are referred to the center. About 63% of the patients were widowed or single, 36% lived alone, and 26% lived with relatives. An increasing percentage of ambulatory patients are being referred to the center. During the early experience one-half of the patients referred were bedfast, while in 1956 this percentage has shrunk to ⅒ of total referrals.

Factors which might explain this trend have been an increased bed capacity in the voluntary chronic disease hospitals, the setting aside of 20 new long-term beds in two general hospitals in the city, and, on a broader scale, a growing recognition on the part of agencies and individuals that bed care is not always the best answer to needs of the long-term patient. Table 3 shows the characteristics of patients newly referred to the center during 1956 by age, degree of disability, living arrangements, financial status, and other factors.

TABLE 3.—*Characteristics of New Patients Referred to Center in 1956*

Sex	Patients, No.
Male	471
Female	858
Age	
<25	19
25-44	68
45-64	233
>64	970
Not recorded	39
Average age	71.6
Marital status	
Married	317
Single	190
Widowed	646
Divorced or separated	79
Unknown	97
Living arrangements	
Alone	487
With spouse	294
With relatives	352
With friends	32
Boarding or nursing home	57
Hospital	29
Other institutions	30
Unknown	18

Degree of disability	Patients, No.
Bed	135
Ambulatory	682
Semiambulatory	184
Unknown	28
Main source of income or support	
Spouse	85
Other relatives and/or friends	156
Old Age Assistance only	46
Old Age Assistance supplemented by relatives, OASI, etc.	203
Other public welfare	22
Pensions (retirement, veterans, etc.)	176
OASI, OASI & savings, relatives, friends	171
Business, employment, rentals	145
Savings only	128
Capital assets, convertible property	48
Disability and unemployment insurance	15
No income	14
Source unknown	120

Needs of Patients

During 1956, requests for 24-hour nursing or supervisory care accounted for a little over 60% of all needs for service among newly referred patients. The next most frequent requests were for counseling and for some type of housekeeper-attendant service. Other requests were for general information on facilities and resources for long-term care, information on a specific facility or resource, or for consultation. Table 4 shows the nature of requests for service received by the center during 1956, divided by new and recall patients.

Problems and Developments

In answering these requests and in attempting to find and effectively utilize existing services and facilities, the center has brought into clearer focus some of the more pressing problems in meeting chronic illness needs in San Francisco.

One of the major problems encountered by the center has been the inability of many patients to pay for the type of care they need. The trouble lies not so much in a shortage of good nursing homes, boarding homes, and other long-term facilities as in the fact that the rates at these better facilities are too often beyond the patient's ability to pay. This has been true both for patients seeking 24-hour nursing care and for those seeking domiciliary or boarding home facilities.

The center has also found that there is not enough provision for rehabilitation in the various long-term facilities. In the proprietary nursing and boarding homes the emphasis given to rehabilitation varies widely and reflects the philosophy of the operator, his idea of the rehabilitative potential of the elderly chronically ill person, and the economic effect such services will have on his own business. Consistent physical and occupational therapy and diversional programs are for the most part lacking in proprietary facilities for long-term care, where the lack of adequate staff and the cost of such services prohibit organized efforts.

TABLE 4.—*Nature of Patient Requests, 1956*

		New Cases	Recalls	Total
Nursing home, boarding home, institution		819	228	1,047
Housekeeper, attendant, etc.		142	51	193
Information re facilities and resources				
Sheltered or home employment	13			
Financial assistance	11			
Wheel chairs, hospital beds, etc.	11			
Rehabilitation services	7			
Medical and dental care	10			
Free or cheaper medicine	11			
Housing	12			
Transportation to clinic	10			
Recreation & companionship	8			
Day care (custodial)	3			
Restaurants serving special diets	2			
Misc. procedures, legal advice, camp, etc.	12			
Total		110	42	152
Information on specific facility		56	51	107
Consultation		52	54	106
Counseling		150	107	257
Additional information only*		...	369	369
Total		1,329	902	2,231

* Applies to recalls only.

Considerable overlapping and duplication of function exists among the various chronic disease facilities and services. No facilities especially adapted to the needs of the younger chronically ill adult presently exist. There are limited subsidized convalescent resources for women and none for men in the city.

Another problem has been obtaining efficient, reliable homemaker-attendant services. Previous attempts at homemaker service for the city's chronically ill have been sporadic and temporary in nature, and there is no permanent, established program of this type at the present. (A limited demonstration Homemaker Service primarily for chronically ill and aged persons was established on May 1, 1957.) As a result, the cost of obtaining reliable full-time attendant service has been prohibitive for many families, and the type of consistent, dependable part-time help which would make secure family planning possible has been equally hard to find.

Another need that has become increasingly clear as operations progressed is for more counseling specifically geared to the chronically ill, embracing the many problems that accompany long-term sickness or disability, such as dwindling finances, family attitudes, living arrangements, and the psychological impact of long-term dependency. The center reports that there has not been too much change in the types of patients or problems since its inception, but there has been encouraging progress in the community's thinking about chronic illness. Some change is evident in the "hopeless" pattern of patient management and more emphasis is being placed on rehabilitation.

Services to the Community

As the result of its contacts with patients and its work and findings in the community, the center has been able to implement and participate in broader community planning for service to the chronically ill. In addition to maintaining complete information on the services, rates, and facilities in commercial nursing and boarding homes in the San Francisco area, the center has sponsored two institutes for nursing and boarding home operators. The second in a series of five meetings, held in the fall of 1955 by popular request of the operators, featured demonstrations and discussion of new techniques in patient management. The center also continues to provide consultation on standards of care and operating practice to operators on a day-to-day basis, and to sponsor a closer working relationship between nursing and boarding homes and hospitals, physicians, and other related organizations.

Partly as a result of the center's recommendations, and with its informal participation, a home-care plan for the chronically ill of San Francisco is in operation at the Mount Zion Hospital, and the Center has continued to stimulate the formation of other such programs, particularly under public auspices. Finally, the center continues to bring together representatives of the voluntary health organizations concerned with long-term illness and has provided these organizations with a basis for joint planning and action.

MEDICINE AND THE LAW

AVERTING PROFESSIONAL LIABILITY ACTION

Samuel Polsky, Philadelphia

There are three fallacious attitudes common among doctors that lead to professional liability action. First is the belief that diagnostic and surgical skills are the chief safeguard against a malpractice action; second, that being a good Samaritan is good medicine; and third, that a just cause is a good cause. These virtues may win lawsuits, but they seldom prevent them. Being a defendant in a malpractice action is never a happy experience, no matter how sweeping the ultimate victory may be. Before I am branded as a devil's advocate or dismissed as a complete legal cynic, let me still some of the free-floating anxiety that the word "malpractice" seems to arouse in physicians by stating that the bulk of malpractice actions in the United States are readily preventable.

For proof of that statement one need only look at the medical quack. Of the tens of thousands of malpractice actions that fill our law reports, how many are directed against quacks? Disconcertingly few. What accounts for this peculiar state of affairs? It cannot be explained away by saying that there are relatively few medical quacks left; that may be true in some parts of the country but false in others. The efforts of medical societies and the work of the United States postal authorities, the Pure Food and Drug Administration, and other agencies testify to a continuing fight against new medical quacks as fast as the old ones are put out of business. But almost without exception public or quasi-public agencies such as the medical societies conduct the fight. Rarely does the individual victim bring a malpractice suit against the medical quack.

The reason for this is not difficult to find. The only skill that the quack has to sell is the ability to establish and maintain rapport with another person. Medical skill is completely absent, yet so are malpractice suits.

As a case in point, some years ago in Pennsylvania a self-styled plastic surgeon set up in business. He straightened noses by injection of wax. Unfortunately, on hot July days, his patients found their noses melting. They did not run to their lawyers, however. There was no need to; day or night their "doctor" was available with sympathy, consideration, and understanding and ultimately, of course, with more artistry in wax. The medical society fought him through one court after another, but not even this publicity was enough to break his immunity from malpractice attacks by his victims.

His single stock in trade was an excellent bedside manner, reflected in a continuing high degree of rapport with his patients. This was enough to prevent malpractice actions despite his complete absence of formal medical training. This is not to suggest that medical schools establish a clinical professorship in medical quackery to teach the skills of rapport. All too often, however, this skill tends to be dwarfed by other professional skills. Perhaps, also, the association of this one skill with the quack leads to its depreciation in the hands of the reputable physician. To some extent the demands of a busy practice accomplish the same result, and specialization exacts somewhat the same toll.

I suggest that the modern surgeon exhibits little warmth in establishing the physician-patient relationship. May I also suggest that it is this factor, rather than the risks inherent in surgery, which so often makes the surgeon the target of malpractice litigation? The risks of surgery are not to be denied, of course, but that very fact conditions the patient to accept an untoward result with greater tolerance. If I were required to state a first principle of preventive law in malpractice actions it would be that diagnostic and surgical skills are far less important than is skill in establishing a friendly physician-patient relationship. In achieving this, it seems to me that the ability to listen and simply being available to the patient are all-important.

There is a difference, of course, between being a good doctor and being a good Samaritan. The second legal pitfall leading to a malpractice action lies precisely here. The physician should exercise his bent for doing good in the highest tradition of his profession by giving of his services as freely as he likes or is able; he enters dangerous ground only when he stops practicing professional medicine in order to practice amateur economics. The warning signs and admonitory symptoms are plain. They may be summed up as hypersensitivity of the ego accompanied by subacute melancholia and manifested by Hamlet-like musings along these lines: Can the patient really afford a roentgenogram?

Associate Professor, Temple University Law School, and Director, Philadelphia Medico-Legal Institute.

Read before the forum The Doctor and His Practice, presented by the Wm. S. Merrell Company and the Erie (N. Y.) County Medical Society, Buffalo, Nov. 6, 1958.

Will he think I am just trying to squeeze another visit out of him if I ask him to come back for a follow-up examination? Is it an admission of failure if I suggest a consultation? The variations are infinite, but the basic syndrome remains one of medical insecurity largely induced by economics. It results in indecision and lack of medical action and is defensively rationalized as concern for the patient. The diagnosis is cardiovascular good-Samaritanism.

The prognosis is guarded, with possible legal complications which often take the form of a malpractice action based on failure to check routine safeguards, failure to follow up, failure to obtain consultation, failure to refer the case for observation or specialized treatment, failure to advise the patient of the risks of inaction, and sometimes even failure to tell the patient just how ill he really is.

If, therefore, I had to state a second principle of malpractice prevention it would be to diagnose and cure yourself of good Samaritan palpitations unless you would like to recite and explain your soliloquies from the witness stand to a patient you have abandoned medically. This is not overstating the case, for opposing counsel and the court will remind you (and the audience of 12 jurors) that good intentions are not the equivalent of good medical practice.

The third fallacious attitude that I would invite you to consider is that a just cause is a sound course to pursue. The history of many malpractice actions begins with the righteous indignation of a physician whose fees have not been paid by a patient who can afford to pay them. After a course of polite and then pointed reminders have failed to elicit response the matter is turned over to a commercial collection agency, whose insistence reminds the patient so often of the doctor that in time he develops at least a mild obsessive-compulsive neurosis. The obsession takes the form that the doctor is not, and never was, any good. In time this includes the view that the physician lacks skill as well as being a money-mad pirate without principles or scruples. The compulsion takes the form of a desire to talk about the persecution to all who will listen. The patient's family and friends assure him that he is right and that he looked, talked, and felt far worse after the doctor's shameful treatment and incompetent ministrations. Soon the patient thoroughly believes all this, and the obsession has become a delusion with strong paranoid coloring. By the time he sees his first lawyer he is thirsting for primitive retaliation. After being told he has no case, he broods over the deficiencies in his cause of action and eventually comes to discover the missing elements. The next lawyer he sees has a case that spells legal indignation over medical malpractice, and suit is started. Or the physician may sue for his bill and by a similar, perhaps more rapid, process find himself faced not only with defense of malpractice but a counterclaim or countersuit for damages.

This history can be altered by a rather simple bit of preventive law: A just cause must not be hurried on its course. The statute of limitations for malpractice actions is far shorter than the limitation period for debts or contracts. Usually the malpractice action must be brought within one or two years of the time of alleged injury, while the debt or fee is not outlawed for some six or seven years from the time when it was contracted. Patience, in waiting until the malpractice period of limitations has run out, will not only restrain unwarranted suits of a purely retributive nature but may even result in peaceful, perhaps piecemeal, payment of the fee.

As a final item of preventive law I urge that writing be retrieved from among the lost arts of medicine. If a patient refuses to follow advice, write and either tell him to get another doctor within a reasonable time or inform him that you cannot and will not be responsible for his treatment if he refuses to take your advice. Also, if you have a seriously ill patient who requires frequent or constant care or may require emergency care while you are away on vacation or on a trip, do not rely on your answering service to do your referrals under such circumstances. A note to the patient, telling him who will be covering your practice in your absence, and a note to the other physician, describing the case and course of treatment, not only will avert malpractice actions but also may prevent serious harm for the patient. And when an experimental or risky procedure is to be tried do not rely on just the hospital release form and the patient's oral consent. His consent, after explanation of the risks, should be obtained in writing. It need hardly be added that it is wise to keep copies of these letters in your own records. The psychological value of such written communications in dissuading a patient from initiating litigation is probably greater than their probative value in court; but that, after all, is simply another way of saying that the measure is good preventive law.

While many (perhaps most) malpractice suits can be prevented, some will always remain. No profession is wholly immune from carelessness or ignorance. I urge in conclusion that, when such a situation arises in your medical community, it is not preventive law to refuse to make your honest opinion known. Refusal to testify under such circumstances involves something more important than personal convenience or lack of fortitude. It defeats justice, and degrades both law and medicine from their high estate as professions worthy of public respect.

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The Roentgen Diagnosis of Lesions of the Spine, Dr. John Arthur Evans, New York City.

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ILLINOIS

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Quincy Physicians Assist New Educational Society.—On March 20 there was born in Quincy a new, nonprofit, international, educational organization called the "Society for Academic Achievement in Secondary Schools." The principal purpose of the new society is "to promote, popularize, and reward high academic scholarship achievement in the secondary schools of the United States and Canada; to guide and motivate superior and talented students to seek a college education." The society is an outgrowth of the Quincy Major Learning Program, dedicated to the guidance and motivation of the students of Quincy and Adams County to seek college education, initiated and sponsored by the Swanberg Kiwanis Foundation and the Kiwanis Club of Quincy in 1956. Community organizations, not affiliated with the secondary schools but approved by the school administrators, are being urged to sponsor the society in the secondary schools. Academic scholarship achievement awards will be given in accordance with regulations established by the society, with the secondary school principal, or his representative, responsible for the faithful observance of the regulations. Each student award recipient becomes an award member of the society for life. The criterion for award membership is competitive high scholarship achievement, especially in academic subjects. The incorporators of the society have adopted a constitution, made application for Illinois incorporation as a nonprofit organization, and elected the first board of trustees. Among the seven incorporators are Dr. Elbert Newton DuPuy, Quincy, counselor, Illinois State Medical Society, and Dr. Harold Swanberg, Quincy, secretary, American Medical Writers' Association and Mississippi Valley Medical Society. The society is being sponsored by the Medical Foundation of the Adams County Medical Society, the Kiwanis Foundation of the Kiwanis Club of Quincy, the Collegiate Educational Fund of the American Medical Writers' Association, and the Mississippi Valley Medical Society. The sponsors are nonprofit organizations, which have education as one of their objectives and each has given a grant to get the new society launched.

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MEDICAL NEWS

ALABAMA

Dr. Spies Honored.—For the first time, an "International Boss of the Year" was selected by The National Secretaries Association (International). The honor went to Dr. Tom Spies, of Birmingham, director of the Nutrition Clinic at Hillman Hospital and chairman, department of nutrition and metabolism, Northwestern University Medical School, Chicago. The award was presented to Dr. Spies during Secretaries Week, on Secretaries Day, Wednesday, April 22. Dr. Spies' background was submitted for the "International Boss of the Year" award by his secretary, Miss Margaret Owen, of the Birmingham Chapter, National Secretaries Association.

Clinical Meeting Held at the Tuskegee Institute.—The 47th annual meeting of the John A. Andrew Clinical Society was held April 12-17 at the John A. Andrew Memorial Hospital, Tuskegee Institute, under the presidency of Dr. J. D. Merida, Cleveland. Over 30 papers were presented, including the Charles R. Drew Memorial Lecture given by Dr. Hollon W. Farr. A Medical-Dental Lecture, "Cancer of the Mouth," was also presented by Dr. Farr. Panel discussions were held on "Drug Therapy of Hypertension" and "The Use of Tranquilizing Drugs." A clinical pathological conference, movie sessions, and a clinical case presentation on "Sarcoidosis–Hodgkin's Disease" were held. At the banquet April 13, Commissioner Elmer A. Carter, State Commission Against Discrimination, New York City, presented an address.

CALIFORNIA

Los Angeles Doctors' Symphony Orchestra.—This organization held its annual elections recently and the following are new officers: Dr. Lester M. Morrison, president; Dr. Jesse Younger, vice-president; William Curry, D.D.S., secretary; Dr. John Brody, treasurer; Mrs. John Brody, librarian. The Los Angeles Doctors' Symphony Orchestra is a five-year-old, nonprofit organization sponsored by the Los Angeles County Medical Association which holds weekly rehearsals and gives two symphonic concerts yearly for charitable purposes. The orchestra consists of 80 musicians, composed of physicians, dentists, and allied professionals "who have banded together in a merger of medicine and music for mutual enjoyment." A concert held Jan. 21 in Philharmonic Auditorium was given for the use of the City of Hope with Anna Maria Alberghetti as guest artist. The next spring concert is scheduled for June 6.

DISTRICT OF COLUMBIA

Dr. Bayne-Jones to Receive Award.—The Board of Directors of the Passano Foundation announce that Dr. Stanhope Bayne-Jones has been selected as the recipient of the $5,000 Passano Award for 1959. On Wednesday evening, June 10, during the convention of the American Medical Association in Atlantic City, a reception and dinner will be held at the Traymore Hotel to honor Dr. Bayne-Jones. Dr. Louis M. Orr, incoming President of the A. M. A., will speak on Dr. Bayne-Jones' contribution to the practice of medicine. Joseph C. Hinsey, Ph.D., director, New York Hospital–Cornell Medical Center, New York City, will present Dr. Bayne-Jones' contribution to medical education. This year's award is presented to Dr. Bayne-Jones "in recognition of a long and extraordinary service to science and medicine as educator and administrator in tasks of the highest importance, in all of which he has served with distinction and faithfulness." His most recent post was that of chairman of the Secretary's Consultants on Medical Research and Education, Department of Health, Education, and Welfare. The Passano Foundation was formed late in 1943, having as its sole purpose the encouragement of medical science and research, particularly that having a clinical application. It is sustained by annual contributions from The Williams & Wilkins Company, publishers of medical and scientific books.

GEORGIA

Annual Session in Augusta.—The 105th annual session of the Medical Association of Georgia will be held at the Bon Air Hotel, Augusta, May 17-20. The House of Delegates will convene May 17, 5 p. m., and reconvene May 20, 9 a. m. Dr. Paul Dudley White, Boston, will present the Association Abner W. Calhoun Lectureship, "Cardiovascular Disease in the Light of the Long Follow-Up," at noon, May 19. Papers by guest speakers will include the following:

Fire and Exposure Hazards in Hospitals and Their Control, Dr. George J. Thomas, Pittsburgh.

The Inadequacies of Routine Bleeding and Clotting Time Determination, Dr. Louis K. Diamond, Boston.

The Radiologist and the Film Processing Problem, Mr. William H. Ramey, Rochester, N. Y.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Clinicopathic Meaning the Nephrotic Syndrome, Dr. Arthur C. Allen, Miami.

The Roentgen Diagnosis of Lesions of the Spine, Dr. John Arthur Evans, New York City.

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Personal.—Dr. Manuel E. Lichtenstein has been elected chairman of the department of surgery, Cook County Hospital. He was also elected to membership on the board of trustees, Cook County Graduate School of Medicine.—Dr. Piero P. Foa, professor of physiology and pharmacology, Chicago Medical School, will address a series of seminars at the Universities of Copenhagen, Helsinki, Edinburgh, and Milan, during April and May. He will also address an International Symposium on the Relationship of Sulfur to Diabetes at the University of Bologna.

LOUISIANA

Meeting of State Society in New Orleans.—Physicians from all 64 Louisiana parishes will meet in New Orleans May 4-6 for the 79th annual meeting of the Louisiana State Medical Society. Dr. Gunnar Gundersen, LaCrosse, Wis., President of the American Medical Association, will address the opening meeting May 4. Dr. William C. Rivenbark will be general arrangements chairman for the meeting, and Dr. Arthur D. Long Jr., of Baton Rouge, president of the Louisiana State Medical Society, will preside. Among the out-of-state guest speakers who will address scientific sessions are Dr. Edward S. Judd Jr., Rochester, Minn.; Dr. Samuel Buford Word, Birmingham, Ala.; Dr. David G. Decker, Rochester, Minn.; Dr. E. Crampton Harris Jr., Mobile, Ala.; Dr. Theodore C. Panos, chairman, department of pediatrics, University of Arkansas Medical School, Little Rock; and Elaine L. Updyke, Sc.D., Atlanta, Ga. Louisiana State Medical Society members completing 50 years of medical practice will be given special recognition at the opening meeting and be admitted to the "50-Year Doctors Club." A full schedule of scientific and business discussions will be conducted during the three-day meeting. All sessions will be held at the Roosevelt Hotel. For information, write the Louisiana State Medical Society, 1430 Tulane Ave., New Orleans.

MASSACHUSETTS

Medical History Lecture.—A new Horblit Lecture on the History of Science was inaugurated at Harvard University, Boston, by Herbert Butterfield, Master of Peterhouse and the professor of modern history at the University of Cambridge, England. "The History of Science and the Study of History" was Professor Butterfield's subject at 8 p. m., March 24, in the Allston Burr Lecture Hall. The new Horblit Lecture on the History of Science is supported by a fund established by Mark M. Horblit, of Newton Center, Harvard alumnus.

Personal.—Dr. W. Bradford Patterson, of Wellesley, has been appointed chief of professional services at Pondville State Hospital, Dr. Alfred L. Frechette, commissioner, Massachusetts Department of Public Health, has announced. Dr. Patterson will take over some of the duties of Dr. Ernest M. Daland, chief of staff, who has held this position since the hospital was established 32 years ago. Dr. Daland is planning to retire from Pondville and is turning over his duties gradually, but will continue as an executive member of the consulting staff.—Dr. Alfred Hollander, assistant professor of clinical dermatology, Boston University School of Medicine, presented "Diagnosis and Therapy in Dermatology" under the auspices of the World Medical Association before the Peruvian Medical Association in Lima, Peru, in March. He also spoke before the Peruvian Anatomico-pathological Society on "Newest Histopathological Findings in Dermatology."

Break Ground for Research Building.—Ground was broken March 2 for a 3-million-dollar medical research building for the Boston University School of Medicine. The site of the projected building is adjacent to the School of Medicine at 80 E. Concord St. and is bounded by East Concord and Stoughton streets and Harrison Avenue. President Harold C. Case, of Boston University, spoke during the informal ceremony. Invited guests included the university's four vice-presidents: J. Wendell Yeo, Ph.D., vice-president for student affairs; George A. Warmer, D.D., vice-president for university affairs; John A. Dunn, vice-president for university development; and Kurt M. Hertzfeld, vice-president for administrative affairs. Other invited participants were Dr. Chester S. Keefer, dean and director of the School of Medicine; Dr. Lamar Soutter, associate dean; Randall W. Weeks, executive secretary of the university's General Alumni Association; and Russell W. MacLaren, business manager of the university. The building, which will take 18 months to complete, will be devoted to research and clinical and basic medical sciences.

MICHIGAN

Service for Multiple Sclerosis Patients.—A consulting and diagnostic service for multiple sclerosis patients has been established at Wayne State University College of Medicine, Detroit, according to Dr. John S. Meyer, chairman, department of neurology. The service is sponsored by a $20,000 grant from the Michigan Chapter, National Multiple Sclerosis Society, a United Fund–Torch Drive Agency. Dr. John T. McHenry, associate professor of neurology, is director of the new Multiple Sclerosis Clinic. The department of neurology will provide neurological supervision and clinical evaluations for the referring physician. Research projects will be conducted by the department. Physical therapy and related treatments will be administered at the Rehabilitation Institute of Metropolitan Detroit and other community rehabilitation agencies.

MINNESOTA

Dedicate Hall Honoring Dr. Diehl.—Dr. Harold S. Diehl, dean emeritus of the University of Minnesota College of Medical Sciences, Minneapolis, was honored recently at a medical symposium and dedication of a new medical school building named Diehl Hall. The $2,750,000 building will be completed next fall and will house the university's medical-biological library and medical research facilities. Dr. Diehl is now residing in New York City, where he is senior vice-president for research and medical affairs and deputy executive vice-president of the American Cancer Society.

Report on Decrease in Syphilis.—*Minnesota's Health*, a publication of the Minnesota Department of Health, has reported that four decades ago, venereal disease was a serious problem in Minnesota. Since then, congenital, neural, and infectious syphilis have been virtually eliminated and the number of reported resident cases of syphilis of all types cut from a peak of 4,300 and a morbidity rate of 173.3 per 100,000 population in 1925 to a record low of 137 reported cases and a provisional morbidity rate of 4.0 per 100,000 in 1958. In the first quarter of the latter year, the state's rate was 5.3, a figure lower than in 45 other states, according to U. S. Public Health Service statistics. Had the 1925 rates continued unabated, the state would have had an estimated 5,830 resident cases of syphilis in 1958, a figure more than 40 times the actual number. Most cases of the disease are now discovered and treated in time to prevent late active, cardiovascular, neural, and congenital syphilis. The "failure rate" (late active and congenital syphilis per 100,000 population) dropped from 32.0 in 1940 to 3.5 in 1952, the last year for which such statistics are available. Only 20 infectious cases were reported during 1958, and the state reportedly was the first in the nation to go through an entire year(1950) without a newborn luetic birth. An occasional congenital case involving older persons still appears, however. Sixty cases were reported in 1946, only four in 1958. Since 1953, there have been no reported resident cases involving the newborn. Deaths with syphilis as a major or contributory cause have been four to five times lower than rates of 25 years ago. During 1957, deaths in which syphilis was the major cause totaled 39.

NEBRASKA

Annual Session in Omaha.—The 91st annual session of the Nebraska State Medical Association will be held April 27-30, at the Hotel Paxton, Omaha, according to Dr. Fay Smith, Imperial, president of the association. Activities include scientific programs, meetings of the governing bodies, and "Sportsman's Day." The meeting will be officially opened April 28 with the presidential address, followed by the installation of the incoming president for 1959-1960, Dr. Ezra E. Koebbe, Columbus. Highlight of the meeting will be the annual banquet at which 29 physicians who have practiced medicine for 50 years will be honored guests and receive 50-year pins in recognition of their service to medicine. Principal speaker for the evening will be Dr. Russell B. Roth, Erie, Pa., who will discuss "A Humorous View of Medical Public Relations." "This meeting will provide all the necessary qualities to give the attending physician a concise and informative program of the latest progress in medicine," Dr. Smith said. Holding their 34th annual meeting will be the Woman's Auxiliary. For information write the Nebraska State Medical Association, 1315 Sharp Building, Lincoln, Neb.

NEW YORK

Chilean Visitor.—Dr. Rafael Darricarrete, director of the School of Medicine of the University of Concepcion in Chile is visiting the New York State University Upstate Medical Center, Syracuse, under a fellowship of the World Health Organization. Dr. Darricarrete is studying the organization of medical education in the United States. He was awarded the WHO fellowship to study plans and methods of teaching in medical schools, curriculum structure, group organization, school organization, and selection of students. Dr. Darricarrete is a professor of bacteriology at the University of Concepcion, and former head of the B. C. G. department, Bacteriological Institute of Concepcion.

New York City

Annual Lecture Given by Dr. Harvey.—The seventh annual Emanuel B. Schoenbach Memorial Lecture was delivered in the Solarium, Kronish Pavilion, Maimonides Hospital of Brooklyn, April 16 by Dr. A. McGehee Harvey, professor of medicine, Johns Hopkins University School of Medicine and physician in chief, Johns Hopkins Hospital, Baltimore. Dr. Harvey's talk was on "Systemic Lupus Erythematosus."

OHIO

Sir Francis Walshe Visits Cincinnati.—On April 25 Sir Francis Walshe, British neurologist who is visiting professor of neurology at the University of Cincinnati College of Medicine and Cincinnati General Hospital, April 17-26, presented a lecture at the Veterans Administration Hospital Auditorium on "Mind and Brain." Sir Francis came to the United States through the joint efforts of the University of Cincinnati, Washington University, St. Louis, and the

University of California, San Francisco. At Cincinnati he conducted conferences, ward rounds, and a neurological clinical pathological conference.

Plan Kettering Memorial Medical Center.—Mr. Eugene W. Kettering, son of the late Charles F. Kettering, inventor, has announced plans to develop a 4-million-dollar medical center, including a 200-bed hospital, medical research building, health museum, and quarters for the Montgomery County Medical Society. The Kettering Memorial Medical Center would be situated on the 90-acre Kettering estate located in Kettering Village adjacent to Dayton and would include all of the estate except the residence and immediate grounds which the family will continue to occupy. Financing will be by friends and associates of the late Mr. Kettering, who have indicated their wish to join in developing the medical center, Mr. Kettering said. The project will take two years to complete after contracts are awarded. The hospital is designed for future expansion to 400 beds. Mr. Kettering, who resides in Hinsdale, Ill., has given a health museum to that community. He said the museum planned for the memorial center would be a facility for public education. The building would also house the Montgomery County Medical Center. The new hospital will be privately administered, and will be operated on the open staff principle whereby any physician may practice there so long as he meets the necessary professional standards. Development of the project is to be under direction of the Montgomery County Foundation for Research and Education, with Mr. Kettering as foundation chairman. Physician members of the foundation include Drs. G. Douglas Talbott, Dayton, and Col. John P. Stapp, Aero Medical Laboratory, Wright Air Development Center.

PENNSYLVANIA

General Practice Meeting in Bedford.—The 11th annual scientific assembly of the Pennsylvania Academy of General Practice will be held April 29-May 2 at the Bedford Springs Hotel, Bedford. Sessions are planned under the following headings:

The Management of Automotive Injuries.
Cardiology.
Ophthalmology.
Office Diagnosis, Therapeutics and Pharmacology.
Trauma.

A Symposium on Pediatrics May 2 will include papers by Dr. Edward Press and Dr. Mary Allen Engle, New York City, Dr. Paul Gyorgy, Philadelphia, and Dr. John Lester Reichert, Chicago. Exhibits are planned and question-and-answer periods will conclude three of the sessions. Ten hours of category I credit by the American Academy of General Practice will be given for attendance. For information write the Pennsylvania Academy of General Practice, 4450 State Road, Drexel Hill, Pa.

SOUTH DAKOTA

Dr. Parke Honored.—Dr. Leroy L. Parke, general practitioner in Canton for 46 years, was named "Man of the Year" by the Canton Chamber of Commerce at its annual banquet at the Masonic Temple Jan. 8. Dr. Parke received a lapel pin proclaiming him as "1958 Man of the Year." He has been mayor of the town, a member of the City Council, and served a number of terms as Republican County Chairman.

Plan Fall Meeting for Hunters.—The Council of the South Dakota State Medical Association has voted to continue its "Fall Hunters' Medical Meeting" in 1959, which combines a medical program with pheasant hunting. Lectures are given each morning and evening with hunting in the afternoon. The meeting is usually held the first five days of the hunting season. Physicians from any part of the country are welcome to attend. Enrollment is limited and applications are handled on a "first come, first served" basis. For information, write Mr. John C. Foster, Executive Secretary, South Dakota State Medical Association, 300 First National Bank Building, Sioux Falls, S. D

WASHINGTON

Swedish Surgeon Named Walker-Ames Professor.—Dr. John Philip Sandblom, president of the University of Lund, Sweden, has been appointed a Walker-Ames Professor of Surgery at the University of Washington School of Medicine, Seattle, for a period of six weeks, during March and April, 1960. Dr. Sandblom, is an honorary fellow of the American College of Surgeons, and is immediate past-president of the Swedish Surgical Society. He is founder of the International Surgical Club, and is the author of more than 70 research papers on surgical subjects. While at the university, Dr. Sandblom will lecture to medical students and residents and will give research seminars and demonstration operations.

GENERAL

Neurological Surgeons Meeting in New York City.—The 50th meeting of the Society of Neurological Surgeons will be held at the Neurological Institute of New York, New York City, April 27-28, under the presidency of Dr. Leonard T. Furlow, St. Louis, who will present "The Neurosurgical Aspects of Neurilemommas of the Seventh Cranial Nerve" the morning of April 28. The institute is celebrating its 50th anniversary. Fourteen papers are scheduled for presentation, including "Neutron Capture Therapy—Promise or Fantasy," by Dr. Lee E. Farr, medical director, Brookhaven National Laboratory, Associated Universities, Inc., Upton, Long Island. An exhibit of early New York neurosurgical contributions has been arranged by Dr. Byron Stookey, Sharon, Conn. Discussions and a ladies' program are planned, and the annual dinner will be held April 27, 7 p. m., at the Waldorf-Astoria. For information write Dr. Bronson S. Ray, 525 E. 68th St., New York 21.

Committee for Information on Alaska.—An Interagency Research Advisory Committee was formed by representatives of the Alaska Department of Health, Alaska Native Health Service (U. S. Public Health Service), Arctic Aeromedical Laboratory (U. S. Air Force), and Arctic Health Research Center (U. S. Public Health Service) for the purpose of assisting scientific investigators in medical and allied fields who may wish to perform research in Alaska. The committee is prepared to assist investigators sponsored by a recognized institution by explaining local situations, in meeting logistic difficulties, and in making available Alaskan facilities. Persons desiring such assistance should write Mr. E. M. Scott, Chairman, Interagency Research Advisory Committee, Arctic Health Research Center, Box 960, Anchorage, Alaska.

Meeting on Goiter in Chicago.—The American Goiter Association will meet at the Drake Hotel, Chicago, April 30-May 2. Over 30 papers are scheduled for presentation including "The Occurrrence of Iodinated Tyrosines in Human Plasma," by Helen E. A. Farran, B.Sc., and R. Bird, Ph.D., London, England, and "Observations Concerning the Free Myo-Inositol of Thyroid Tissue," by Dr. Norbert Freinkel, Dr. Sidney H. Ingbar, Dr. Charles J. Goodner, and Mr. Robert W. White, Boston, and Rex M. C. Dawson, Ph.D., Babraham, Cambridge, England. The presidential address will be given May 1, 2 p. m., by Dr. Warren H. Cole, Chicago, to be followed by the Van Meter prize essay and a round-table discussion, "Thyroid Carcinoma: Morphologic Types and Their Biologic Behavior," moderated by Dr. Lewis B. Woolner, Rochester, Minn. For information write Dr. John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., Secretary.

National Convention on Tuberculosis.—The 1959 annual meetings of the National Tuberculosis Association, the American Trudeau Society, and the National Conference of Tuberculosis Workers will be held at the Palmer House, Chicago, May 24-29. An organizational meeting of the Governing Council of the NCTW is planned. Medical, public health, and nursing sessions will begin May 19, and general sessions will include an opening keynote program that morning. The American Trudeau Society committee and council meetings will be held May 22-24. The Trudeau sessions will include two symposiums: "Pulmonary Emphysema" and "Smoke, Smoking, and Chest Diseases," moderated by Drs. Richard V. Ebert, Little Rock, Ark., and Norton Nelson, New York City, respectively. The Amberson Lecture, "Viral Infections in Man: Problems and Progress," will be given by Dr. Frank L. Horsfall Jr., New York City, and the Robert Keeton Memorial Lecture, "Chronic Bronchitis: Clinical Characteristics, Pathogenesis, and Pathology," will be given by Dr. Charles M. Fletcher, London, England. Case conferences and demonstrations are planned. For information write the National Tuberculosis Association, 1790 Broadway, New York 19.

Surgeons Plan Midsummer Tour.—The International College of Surgeons will conduct a midsummer postgraduate tour, and Dr. Ross T. McIntire, executive director, will be the coordinator. Countries to be visited are the Netherlands, Denmark, Norway, Sweden, Finland, Russia, Austria, Germany, and France. Departures will be from New York July 17 on the S. S. Nieuw Amsterdam or by plane July 24. Tour participants will take in the Amsterdam meeting of the college, July 25-26, and the Helsinki meeting, Aug. 8-9; spend three days in Leningrad, Aug. 11-13, and three days in Moscow, Aug. 15-17; and meet with the fellows of the I. C. S. in Vienna, Aug. 19-20. Plane passengers will return to New York Aug. 27 and boat passengers will arrive Sept. 2. For information, write to Dr. Ross T. McIntire, executive director, International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

Meeting on College Health in Philadelphia.—The American College Health Association will hold its 37th annual meeting at the Warwick Hotel in Philadelphia May 6-9. The speaker at the association banquet, May 7, will be Dr. Richard A. Kern, Philadelphia, emeritus professor of medicine, Temple University School of Medicine, rear admiral, M. C., U. S. N. R., retired, and former president of the American College of Physicians. Dr. Donald A. Dukelow, Chicago, will address delegates during the opening general session May 6. The organization comprises some 300 colleges and universities throughout the United States and Canada, and there are about 500 individual members, most of whom are physicians and nurses engaged in student medicine at the college level. For information, write: Dr. Bruce S. Roxby, Chairman, Committee on Local Arrangements, Temple University Health Service, Broad Street at Montgomery Avenue, Philadelphia 22.

Student Meeting in Chicago.—Scientific papers will be presented by medical students and residents for the first time at the ninth annual convention of the Student American Medical Association April 30-May 3 at the Sheraton Hotel, Chicago. The papers will deal with such medical topics as cancer, hormones, internal parasites, and blood cholesterol levels. Eight medical students and three residents will present their papers at scientific sessions May 1 and 2. Featured speakers will be Dr. Alton E. Ochsner, New Orleans, who will discuss smoking and its relationship to lung cancer at the Saturday session, and Dr. Corbett H. Thigpen, Augusta, Ga., psychiatrist, who wrote "The Three Faces of Eve." Eight scientific exhibits, prepared by students, and four prepared by interns and residents, will be on view during the meeting. The House of Delegates will meet on April 30 and May 3. The Woman's Auxiliary to SAMA will hold its second annual meeting simultaneously. The annual banquet and dance May 1 will feature Carl C. Byers, Cleveland, speaking on "He Who Laughs—Lasts!" The choir from the Wayne State University College of Medicine, Detroit, will sing. A new feature of the meeting will be a photographic salon, which will show pictures of both medical and general interest. For information, write the Student American Medical Association, 430 N. Michigan Ave., Chicago 11.

Meeting on Cleft Palate Rehabilitation.—The 17th annual meeting of the American Association for Cleft Palate Rehabilitation will be held April 30-May 2 at the Sheraton Hotel, Philadelphia, under the presidency of Jack Matthews, Ph.D., Pittsburgh. April 30 will be devoted to a short course on problems associated with rehabilitation of individuals with cleft lips and palates and will include round-table discussions. The general sessions will include the following papers by foreign authors:

Cephalometric Measurements on Adult Patients with Unoperated Cleft Palates, Drs. Fernando Monasterio and Alfonso Serrano Rebeil, Mexico, D.F., Mexico.
Cleft Lip and Palate in Twins and Offspring of Twins, Elizabeth Curtis, M.A., Toronto, Canada.
Speech Analysis of Over 20 Children, Prior and Following Pharyngeal Flap Type Repair, Margaret Hamlen, L.C.S.T., Toronto, Canada.

The annual business meeting is planned for 3:30 p. m., May 1. Fee for nonmembers is $3. For information, write D. C. Spriestersbach, Ph.D., Department of Otolaryngology, University Hospitals, Iowa City, Iowa, Secretary-Treasurer.

Training Program in Steroid Biochemistry.—The Worcester Foundation for Experimental Biology, Shrewsbury, Mass., with the department of chemistry, Clark University, Worcester, Mass., and the department of biochemistry, College of Medicine, University of Utah, Salt Lake City, announced the 1959-1960 session of the Training Program for Steroid Biochemistry. "To alleviate the shortage of qualified trained personnel in steroid research," a program will be sponsored by the U. S. Public Health Service through the National Cancer Institute, National Institutes of Health. The courses will stress both theoretical and practical aspects as well as specialized laboratory techniques in steroid research. Postdoctoral candidates (M.D. or Ph.D.) selected for admission both at Worcester and Utah will receive stipends of $5,500 for one year. Predoctoral candidates (B.S., M.S., or equivalent) selected for admission (only at Worcester) will receive stipends of $1,800 for a six-month period. Send inquiries and requests for applications to: Dr. Kristen Eik-Nes, Department of Biochemistry, College of Medicine, University of Utah, Salt Lake City. Classes start Oct. 1. Final date for completion of application is June 1.

Meeting of Pediatricians.—The 69th annual meeting of the American Pediatric Society will be held May 6-8 at The Inn, Buck Hill Falls, Pa., under the presidency of Dr. Joseph Stokes Jr., who will present the presidential address May 6, 8 p. m. Guest speaker at the first session will be Dr. George Siim, State Serum Institute, Copenhagen, Denmark, will present "Studies on Acquired Toxoplasmosis." Of the 97 papers scheduled for presentation the following include foreign authors:

Relation of Intracellular Ions to Metabolite Sequences in Kwashiorkor, Drs. Jack Metcalf, Chicago, Silvestre Frenk, Mexico, D.F., Mexico, and Irena Antonowicz, M.S., Boston.
Motions of the Pharynx and Larynx with Aeration of the Lung at Birth, Drs. James F. Bosma, Salt Lake City, Utah, and John Link, Stockholm, Sweden.
Familial Pulmonary Fibrosis and Its Relationship with the Hamman-Rich Syndrome, Drs. Bernard Laski, W. L. Donohue, J. D. Munn, and Irene Uchida, Ph.D., Toronto, Canada.

A business meeting is planned for May 7, 8:30 p. m. For information write Dr. Aims C. McGuinness, Secretary-Treasurer, American Pediatric Society, 2800 Quebec St., N. W., Washington 8, D. C.

Dr. Boggs to Direct Fund for Education.—Dr. Robert Boggs was appointed director of the Basic Medical Research Program by the National Fund for Medical Education. The Medical Research Program, recently organized by the national fund, will administer funds raised by local United Funds and Community Chests, affiliated with the United Community Funds and Councils of America, for support of fundamental basic research on a national scale. The fund reportedly will not compete with the national voluntary health agencies which sponsor large numbers of research projects in specific fields, "but rather will complement the basic research activities which are a part of these programs by initiating research principally in areas that are not ordinarily covered by specific research projects." Dr. Boggs is a former dean of the New York University Post Graduate Medical School where he served from 1948 to 1955. He is chairman of the National Committee for Resettlement of Foreign Physicians and a consultant on medical projects of the Unitarian Service Committee. In 1959, the National Fund for Medical Education will award grants of over 3 million dollars to the medical schools, bringing to nearly 19 million dollars the total awarded since 1951, when the first grants were made.

Grants to Aid School Faculties.—Twenty-five physicians, teachers, and research workers on the faculties of medical schools in the United States and Canada were appointed Markle Scholars in Medical Science by the John and Mary R. Markle Foundation, New York. Each appointment carries with it a $30,000 grant, appropriated to the medical school where the scholar will teach and do research, to be used toward his support and to aid his research. In the 12 years the fund has been making the scholar grants, over 250 doctors in 74 medical schools in the U. S. and Canada have been aided with total appropriations of $7,550,000. The purpose of the program is "to strengthen medical education by offering academic security and financial help to teachers and investigators in medical schools early in their careers." There were more applicants for the grants this year than ever before. The 25 scholars were selected from nominees from 65 medical schools by five committees of educators and other professional men through extended interviews over three-day periods. The John and Mary R. Markle Foundation was established in 1927 by the late John Markle, Pennsylvania coal operator, "to promote the advancement and diffusion of knowledge . . . and the general good of mankind."

Awards for Heart Research.—The American Heart Association announced the award of $1,562,243 to 182 scientists engaged in a broad range of research studies, most of them in the category of basic research, aimed at pinpointing the underlying causes of heart and blood vessel disease. The awards, which went to individuals in 28 states, the District of Columbia, and two foreign countries, are for 12 months, beginning July 1. Dr. Francis L. Chamberlain, San Francisco, president of the association, pointed out that the awards were made possible through public contributions to the annual Heart Fund appeal. They represent the first part of the 1959-1960 national research support program in which the national office of the American Heart Association participates jointly with its state and local affiliates. A second group of awards, representing grants-in-aid, will be announced in the near future. The fellowship awards just announced include provision for the association's six "career investigators," scientists selected to receive support throughout their productive lives. Also named were 83 "established investigators." This category of award provides five years of uninterrupted support to mature scientists conducting independent programs of research. Ten established investigators also received supplementary grants to help underwrite the costs of technical assistance, equipment, and supplies required for their research. Also named were 45 scientists as "advanced research fellows" and 48 as "research fellows."

Conference on World Health.—The second National Conference on World Health will be held at the Statler Hotel in Washington, D. C., May 7-9, under the chairmanship of Dr. Milton S. Eisenhower, president of the Johns Hopkins University, Baltimore. Among those scheduled to speak is the President of the United States. Arthur S. Flemming, Secretary of Health, Education and Welfare and Dr. Leroy E. Burney, Surgeon General, U. S. Public Health Service, and leaders in public health, medicine, science, and industry will participate as speakers or discussion leaders. Dr. Abraham Horwitz, director, Pan American Sanitary Bureau, Regional Office of the World Health Organization, will speak. Special topics will be taken up in panel discussions and study groups which will report at the end of the conference: (1) prospects for an International Health Year; (2) health and economic development; (3) health and the American image abroad; (4) problems of health in relation to population changes; (5) training and exchange programs of public health personnel; (6) international health and medical research; and (7) the role of nongovernmental health organizations and individuals in the international promotion of public health. Any interested person may take part in the forum discussions and working parties of the conference. Registration will be May 7, 10 a. m.-2 p. m. The fee is $3. Students may register free. The conference is held under the sponsorship of the National Citizens Committee for the World Health Organization, which sponsored the first National Conference on World Health in Washington in 1953. For information, write Mr. Philip E. Nelbach, Executive Secretary, National Citizens Committee for the WHO, 1790 Broadway, New York 19, N. Y.

Society News.—Dr. Lester R. Dragstedt, professor of surgery, University of Chicago, was reelected president of the **National Society for Medical Research.** Also reelected were vice-president, Dr. Alfred Blalock, chief of surgery, Johns Hopkins University, Baltimore; and secretary-treasurer, Dr. Louis N. Katz, head of cardiovascular research, Michael Reese Hospital, Chicago.——The **Mississippi Valley Medical Society** elected the following officers for 1959: president-elect, Arkell M. Vaughn, Chicago; Illinois vice-president, Frank H. Fowler, Chicago; Iowa vice-president, William J. Wolf, West Union; Kansas vice-president, Clarence H. Benage, Pittsburg; Minnesota vice-president, Jacob A. Bargen, Rochester; Missouri vice-president, Barney W. Finkel, St. Louis; Nebraska vice-president, Clyde L. Kleager, Hastings; North Dakota vice-president, Reuben H. Waldschmidt, Bismarck; South Dakota vice-president, Alonzo P. Peeke, Volga; Wisconsin vice-president, Wallace S. Marshall, Watertown; secretary-treasurer, Harold Swanberg, Quincy, Ill.; assistant secretary-treasurer, Preston C. Hall, St. Louis; accounting officer, Jacob E. Reisch, Springfield, Ill. The 24th annual meeting will be held at the Hotel Chase, St. Louis, Sept. 29-Oct. 1, immediately preceding the American Medical Writers' Association meeting Oct. 2-3. The 1959 president is Dr. Arthur F. Fritchen, Decorah, Ia., trustee, Iowa State Medical Society, elected Nov., 1957.—Dr. Cecil M. Kohn, of Kansas City, Mo., was named president of the **American College of Allergists**, at the 15th annual congress of the college, succeeding Dr. Merle W. Moore of Portland, Ore. Named president-elect is Dr. Giles A. Koelsche, Rochester, Minn. Other officers include Dr. Philip M. Gottlieb, Philadelphia, first vice-president; Dr. William B. Steen, Tucson, Ariz., second vice-president; and Dr. Meryl M. Fenton, of Detroit, secretary.—The **Rocky Mountain Radiological Society** has elected the following officers: Drs. George A. Unfug, Pueblo, Colo., president; Gerald S. Maresh, Denver, president-elect; Peter E. Russo, Oklahoma City, Okla., first vice-president; Paul E. Re Pass, Denver, second vice-president; John H. Freed, 4200 E. Ninth Ave., Denver 20, secretary-treasurer; and H. Milton Berg, Bismarck, N. D., historian. The 1959 meeting will be held at the Shirley–Savoy Hotel, Denver, Aug. 20-22.

CANADA

Laurentian Hormone Conference.—The 1959 Laurentian Hormone Conference of the American Association for the Advancement of Science will be held at Mont Tremblant Lodge, Mont Tremblant, Quebec, Aug. 30-Sept. 4. Investigators interested in attending this conference should apply to the Committee on Arrangements, Laurentian Hormone Conference, 222 Maple Avenue, Shrewsbury, Mass. The conference is arranged under four general headings: Mechanism of Hormone Action, Peptide Hormones, Thyroid Hormones, and Hormones and Metabolism. Papers by foreign participants will include "Hormonal Activity of Active Polypeptides," by Hector Croxatto and Livio Barnafi, Catholic University, Santiago, Chile, and "Influence of Hormones on Adipose Tissue as a Center of Fat Transport," H. E. Wertheimer, The Hebrew University–Hadassah Medical School, Jerusalem, Israel. Applications will be screened and invitations issued by the Committee on Arrangements by June 12.

Establish Lectureship in Ophthalmology.—Dr. Walter W. Wright, University of Toronto professor emeritus of ophthalmology, has been honored by a lectureship in his name established with funds raised by department of ophthalmology staff members, former students, and friends. Dr. Wright conceived and developed the postgraduate training of physicians in eye diseases, reportedly the first such training in Canada, which began at the University of Toronto in 1941. Dr. Wright is also consultant to the Canadian National Institute for the Blind, the Toronto General Hospital, and the Hospital for Sick Children. He joined the University of Toronto staff in 1908, served as an ophthalmic specialist in the Canadian Army Medical Corps, returned to the university in 1921, and headed the department of ophthalmology from 1941 until retirement in 1946. The first Walter W. Wright lecture was given by Prof. Norman Ashton, ophthalmic pathologist of the Institute of Ophthalmology, London, England, who spoke on "A New Approach to the Problem of Diabetic Retinopathy" at the Academy of Medicine Feb. 27.

LATIN AMERICA

Cuba Joins Malaria Eradication Drive.—The new Cuban government and the Pan American Health Organization recently pledged themselves to eradicating malaria and the carrier of urban yellow fever in Cuba. The agreement was signed by provisional President Manuel Urrutia and Minister of Health Dr. Julio Martinez Paez for Cuba and Dr. Abraham Horwitz, of Chile, director of the Pan American Sanitary Bureau, regional office for the Americas of the World Health Organization and PAHO's operating arm, for the international health organization. Cuba has supported the resolutions in favor of the hemisphere and global malaria eradication campaigns in Pan American Sanitary Conferences and World Health Assemblies, but only now has it been possible to start on an eradication program. Though begun in 1953, Cuba's efforts toward eradicating the Aëdes aegypti mosquito have been modest, reportedly because of lack of funds. Under the terms of the new agreement they will be expanded.

FOREIGN

Symposium on Sulfur.—The Third International Symposium on Sulfur Therapy will be held in Tabiano and in Salsomaggiore, Italy, May 8-10 on occasion of the inauguration of the new termae of Tabiano "Emilio Respighi." Professors Demenico Campanacci, of the University of Bologna, and Carlo Bianchi, of the University of Parma, will preside. Italian and foreign scientists will participate and will read papers, including Dr. Piero P. Foa, of Chicago, and speakers from Austria, France, Hungary, and Spain. For information, write: Segreteria,

Third International Symposium on Sulfur Therapy, Institute di Patologia Medica, Ospedale Sant'Orsola, Bologna, Italy.

Seminar of Ophthalmology in Tunis.—The first North African Seminar of Ophthalmology will be held in Tunis on May 3-6. The Societe Tunisienne d'Ophthalmologie will meet on the occasion of its third anniversary, and the opening of the Ophthalmological Center will be a part of the seminar, at which Algerian and Moroccan Colleagues, will participate. The subjects will be the following: trachoma; keratoplasty; and recent advances in ophthalmology. Free communications (on internal medicine, ophthalmology, avitaminosis), film projections, and operating sessions will be included. French, English, and Arabic will be accepted for the discussions. Excursions of one or three days will be organized at the end of the meeting. A special program will be prepared for ladies. For information, write Societe Tunisienne d'Ophthalmologie, Le Secretaire General, Dr. R. Mabrouk, Centre Ophthalmologique, Tunis.

CORRECTION

New Mexico Meeting in Las Cruces.—In The Journal, March 28, page 1490, in the Medical News section, sessions for the annual meeting of the New Mexico Medical Society, May 6-7, were listed as being held at New Mexico State University, Albuquerque. This should have read Milton Hall at New Mexico State University, Las Cruces.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8, 1960. Final date for filing application is January 8. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Written.* Several Cities, Oct. 5. *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications is July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates on the West Coast, Portland, Ore., Sept. 9-12. Final date for filing application was March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date far filing application was March 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *I. Oral and Clinical.* Chicago, May 8-19. Formal notice of the exact time of each candidate's examination will be sent him in advance of the examination dates. Candidates who participated in the Part I examinations will be notified of their eligibility for the Part II examinations as soon as possible. Deadline for receipt of new and reopened application for the 1960 examinations is Aug. 1, 1959. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Oral.* Philadelphia, June 2-6; St. Louis, Oct. 6-10. *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 19-21, 1960. The deadline for the receipt of application is Aug. 15, 1959. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 5-9. Final date for filing application is April 1. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pediatrics: *Written.* January 1960. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Written, Part I,* and *Oral, Part II.* Philadelphia, June 12-13. Final date for filing application was February 15. Sec., Dr. Earl C. Elkins, 200 First St., S. W., Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Miami, Fla., Oct. 15-17. Final date for submitting case reports is July 1. Corresponding Secretary, Miss Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Proctology: *Oral and Written.* Philadelphia, September. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New Orleans, Mar. 16-17; Chicago, Oct. 19-20; New York, Dec. 14-15. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Chicago, June 2-4. If needed a special examination will be offered at this time in Nuclear Medicine to diplomates in Radiology or Therapeutic Radiology. The deadline for filing applications is April 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Candidates are urged to apply several months before completion of training requirements although the closing date for filing applications is August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Part II.* Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, September 1959. Final date for filing application is July 1. *Oral.* September. Final date for filing application is July 1. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2, Mich.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application is Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

NAVY

Symposium on Nuclear Medicine.—The United States Naval Medical School, National Naval Medical Center will present its second symposium on advances in nuclear medicine on May 9. This symposium will cover all aspects of the management of the acute radiation syndrome and the care of radiation casualties. The morning session will be devoted to a discussion of low background total body counting, while the afternoon session will cover the diagnosis, management, and treatment of acute radiation syndrome. Authorities scheduled to appear for this symposium are Dr. C. E. Miller, Argonne National Laboratory; Dr. Frederick Reines, Los Alamos Scientific Laboratory; Dr. M. A. Van Dilla, Los Alamos Scientific Laboratory; Dr. R. C. McCall, General Electric Company; Commander H. J. Waters, Technical Assistant for Science Advisor, White House; Dr. Gordon Brownell, Massachusetts General Hospital; Dr. Eugene Cronkite, Brookhaven National Laboratory; Major Kent Woodward, MC, USA, Walter Reed Institute of Research; Dr. Gordon Zubrod, National Cancer Institute; Dr. H. D. Bruner, Division of Biology and Medicine, Atomic Energy Commission; Dr. F. P. Ellinger, U. S. Naval Medical Research Institute; Lieut. Col. Gerald McDonnell, Office of the Army Surgeon General; Dr. Gould A. Andrews, Oak Ridge Institute of Nuclear Studies; and Commander William McFarland, MC, USN, United States Naval Hospital.

There is no registration fee, and all those interested are invited to attend. A special luncheon program, at which Dr. Robert H. Hasterlik of the Argonne Cancer Research Hospital will speak, will be given at the Commissioned Officers' Club, National Naval Medical Center. For further information one may contact the Commanding Officer, U. S. Naval Medical School, National Naval Medical Center.

VETERANS ADMINISTRATION

Big Brother System.—A unique "big-brother" system is being used by hospitalized veterans in their fight against mental illness. Recovering patients at the VA mental hospital in Salisbury, N. C., have formed a society known as "The Helping Hand," in which each member holds himself responsible for more seriously ill patients. Dr. S. J. Muirhead, manager of the hospital, said the society has proved an effective form of help for both its members and nonmembers. Improved patients can help less fortunate patients towards recovery in ways that the hospital staff cannot, since patients ofttimes notice improvement in the condition of their companions and thus become aware that their own improvement is possible. The society's membership is restricted to patients approved by its own screening committee and elected by unanimous vote.

Personal.—Dr. Irvin J. Cohen was appointed assistant chief medical director for planning to succeed Dr. William W. Fellows, who retired in March. Dr. Cohen will direct the medical care program for VA's 171 hospitals, about 100 outpatient clinics, and 17 domiciliary homes. He has been a deputy director for planning since August, 1958.

PUBLIC HEALTH SERVICE

Traineeship in Neurology.—A special traineeship program, under the direction of the National Institute of Neurological Diseases and Blindness, was initiated about three years ago to increase the number of investigators competent to meet the complex problems presented by neurological and sensory disorders. Since its inception, 163 persons have received one to three years of training at 48 institutions in the United States and 16 institutions in seven foreign countries. To qualify for an award, the candidate should have an M.D., Ph.D., or other equivalent degree and at least three years of training or experience pertinent to the training for which he seeks support. The applicant must be a United States citizen or have filed a declaration of intent.

Awards generally are made for not less than nine months and not more than one year, but all awards are subject to renewal for periods up to five years. Stipends are determined individually in accordance with each applicant's qualifications and the financial support needed to obtain the training applied for. Such stipends may range from $6,500 to $17,500 a year. Traineeships frequently are used by basic scientists and clinicians to obtain prolonged and thorough training in highly specialized areas related to their previous experience. For instance, a pediatrician may wish to take specialized training in neurology, ophthalmology, or otolaryngology; and a pathologist, anatomist, or pharmacologist may wish to receive training in the neurological aspects of his discipline. Other candidates seek to increase competence and knowledge in a particular facet of a chosen field for a shorter period. For example, academic and medical faculty members in increasing numbers are using this program to broaden their research experience during sabbatical or other institutional leaves of absence. Requests for complete information about the special traineeship program and application forms should be addressed to Chief of Extramural Programs, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda 14, Md.

DEATHS

Barbour, Fredric Leaworth Ⓜ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; served on the faculty of his alma mater; associated with the Illinois Central Hospital, where he died Feb. 7, aged 74.

Blumenthal, Basil Ⓜ Washington, D. C.; Columbia University College of Physicians and Surgeons, New York City, 1934; specialist certified by the American Board of Internal Medicine; veteran of World War II; clinical assistant professor of medicine; Georgetown University School of Medicine; associated with the Washington General Hospital and the Georgetown University Hospital, where he died Dec. 6, aged 49.

Brown, Charles Arthur, Kansas City, Mo.; University Medical College of Kansas City, 1905; died in the University of Kansas Medical Center Jan. 11, aged 76.

Brown, Grover Cleveland Ⓜ Ste. Marie, Ill.; Barnes Medical College, St. Louis, 1905; member of the American Psychiatric Association; served as managing officer of the Jacksonville (Ill.) State Hospital; at one time district health superintendent for the state; died in St. Anthony Memorial Hospital, Effingham, Nov. 30, aged 73.

Buch, Samuel Montgomery Ⓜ New York City; University and Bellevue Hospital Medical College, New York City, 1905; past-president and charter member of the Bronx Gynecological and Obstetrical Society; consultant, Jewish Memorial Hospital; died Jan. 24, aged 76.

Burnham, Leon Ray Ⓜ Augusta, Maine; Tufts College Medical School, Boston, 1930; veteran of World War II; chief of physical medicine and rehabilitation at the Veterans Administration Center, Togus; died Jan. 21, aged 52.

Burns, Emmet Samuel, Beaver Falls, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1891; died in Ellwood City Jan. 27, aged 90.

Burrows, Byron L., Mount Pleasant, Tenn.; Meharry Medical College, Nashville, Tenn., 1915; died in the Hubbard Hospital, Nashville, Jan. 15, aged 70.

Burton, Robert Elmore, Kingston, Ga.; Eastern University School of Medicine, Baltimore, 1913; past-president of the Bartow County Medical Society; held the post of mayor; served as president of the Kingston Lions Club; died in the Floyd County Hospital, Rome, Jan. 17, aged 68.

Byars, Alfred Henry, Coronado, Calif.; Barnes Medical College, St. Louis, 1898; veteran of World War I; died Jan. 19, aged 86.

Caro, Alfred, Elmhurst, N. Y.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1910; died in the Physicians Hospital, Jackson Heights, Dec. 27, aged 73.

Cary, Raymond John Ⓜ Long Beach, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1912; veteran of World War I; associated with the Seaside Memorial Hospital, where he died Jan. 7, aged 73.

Chalmers, Duncan Macfarlane Ⓜ Long Beach, Calif.; Boston University School of Medicine, 1934; veteran of World War II; certified by the National Board of Medical Examiners; formerly associated with the Indian Service in Juneau, Alaska; died Jan. 10, aged 51.

Cloyd, John Archer, Upper Darby, Pa.; University College of Medicine, Richmond, 1912; for many years a medical officer in the U. S. Navy; served on the staffs of the Presbyterian Hospital in Philadelphia, Bryn Mawr (Pa.) Hospital, and the Delaware County Hospital in Drexel Hill, where he died Jan. 20, aged 68.

Cook, Albert Thomas, Zapata, Texas; Southern Methodist University Medical Department, Dallas, 1912; for many years city and county health officer for Laredo and Webb County; health officer of Zapata County; died in the Mercy Hospital, Laredo, Jan. 21, aged 68.

Cooley, Chester Lynn Ⓜ San Francisco; Stanford University School of Medicine, San Francisco, 1928; specialist certified by the American Board of Obstetrics and Gynecology; on the faculty of the Stanford University School of Medicine; associated with Stanford University Hospitals, St. Elizabeth's Infant Hospital, Children's Hospital, and the Mary's Help Hospital; on the editorial board of the *Western Journal of Surgery, Obstetrics and Gynecology;* died Jan. 22, aged 64.

Corbett, Joseph Horace, Jasper, Fla.; Atlanta College of Physicians and Surgeons, 1901; died Jan. 25, aged 80.

Ⓜ Indicates Member of the American Medical Association.

Counts, William L. Ⓜ Chillicothe, Ohio; Medical College of Ohio, Cincinnati, 1897; an honorary member of the Chillicothe General Hospital staff; died Jan. 12, aged 92.

Cox, J. Emit Ⓜ Fresno, Calif.; Central Medical College of St. Joseph, Mo., 1895; for 30 years member of the board of the Fresno County Tuberculosis Association; at one time practiced in Coalinga, where he was school physician in the Coalinga School District and city health officer; died Dec. 28, aged 93.

Crawford, Georgina Lily Urquhart Ⓜ East Orange, N. J.; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1905; on the medical staff of the New Jersey Bell Telephone Company and Essex County Girls' Vocational School in Newark; served on the staff of Orange Memorial Hospital, where she died Feb. 2, aged 76.

Creskoff, Adolph Jay Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1934; associate professor of clinical medicine at his alma mater; chief of hematology section, Hospital of the University of Pennsylvania; consultant in hematology, Veterans Administration Hospital in Philadelphia; consultant in hematology at the Delaware County Hospital in Drexel Hill, Pa.; died Jan. 22, aged 50.

Darling, Herbert Henry Ⓜ San Rafael, Calif.; Harvard Medical School, Boston, 1925; veteran of World Wars I and II; served as chief of the medical section of the Veterans Administration regional office in San Francisco, where he was formerly on the staffs of St. Francis, Stanford, and Children's hospitals; died Jan. 23, aged 58.

Davies, Daniel Jenkin Ⓜ Cincinnati; Miami Medical College, Cincinnati, 1900; specialist certified by the American Board of Obstetrics and Gynecology; on the faculty of the University of Cincinnati College of Medicine; associated with Bethesda, Deaconess, and Good Samaritan hospitals; died in the Christ Hospital Jan. 27, aged 87.

De Ferari, George Joseph, Brooklyn; University and Bellevue Hospital Medical College, New York City, 1925; interned at St. Vincent's Hospital in New York City; associated with the Brooklyn Doctors Hospital; for many years associated with the Brooklyn Hospital; died Jan. 10, aged 60.

Dickson, Archibald John Ⓜ La Crescenta, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1903; formerly on the staff of the Willard Parker Hospital in New York City; died in the Alta Vista Hospital, Pasadena, Jan. 11, aged 80.

Dixon, William Harvey, Rocky Mount, N. C.; Jefferson Medical College of Philadelphia, 1919; served as medical examiner for the Royal Arcanum for 37 years; died in the Park View Hospital Jan. 23 aged 63.

Dodd, David Wallace Ⓜ Louisville, Ky.; University of Louisville (Ky.) School of Medicine, 1917; veteran of World Wars I and II; assistant chief medical officer for the Veterans Administration; at various times associated with Veterans Administration hospitals in Lexington, Murfreesboro, Tenn., and Nashville, Tenn.; died in the Norton Memorial Infirmary Jan. 15, aged 66.

Dudley, Will Kenney, Paris, Ky.; Kentucky University Medical Department, Louisville, 1904; died in St. Joseph Hospital, Lexington, Jan. 17, aged 80.

Elliott, Joseph Norman Ⓜ Bloomington, Ill.; Northwestern University Medical School, Chicago, 1921; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; associated with the Brokaw Hospital in Normal and the Mennonite Hospital; veteran of World War I; died Jan. 21, aged 64.

Elliot, Robert Edwin Ⓜ Van Nuys, Calif.; Loyola University School of Medicine, Chicago, 1932; on the staff of the Valley Hospital; died Jan. 17, aged 51.

Engelman, Bruno Simon Ⓜ Buffalo, N. Y.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1921; member of the American Academy of general practice; on the staff of the Millard Fillmore Hospital; served a residency at the State Institute for the Study of Malignant Diseases; died Jan. 10, aged 63.

Forsythe, William Alexander, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1917; also a graduate in pharmacy; on the staff of the Mercy-Douglass Hospital; died Jan. 19, aged 74.

Friedman, Harry Falk Ⓜ Miami Shores, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1912; specialist certified by the American Board of Radiology; veteran of World War I; served on the faculty of his alma mater; formerly practiced in Boston, where he was on the faculty of Tufts College Medical School, and was associated with the Boston Dispensary, Westboro (Mass.) State Hospital, Beth Israel Hospital, Massachusetts Memorial Hospital, and New England Hospital for Women and Children; died Jan. 23, aged 68.

Garst, Virgil Paul, Malad City, Idaho; St. Louis University School of Medicine, 1913; Oneida County examining physician for Selective Service inductees during World War II; formerly member of the school board; served on the staff of the Oneida County Hospital; died Jan. 13, aged 78.

Ghering, Harold Alfred Ⓜ Edinboro, Pa.; University of Pittsburgh School of Medicine, 1913; veteran of World War I; for many years physician for Edinboro State Teachers College; on the staffs of the Hamot and St. Vincent's hospitals in Erie; vice-president of the First National Bank; died in the Hamot Hospital, Erie, Jan. 25, aged 72.

Goodwin, Frank Perry Ⓜ Jamestown, N. Y.; Cornell University Medical College, New York City, 1906; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War I; past-president of the Chautauqua County Medical Society; member of the staffs of the Jamestown General and Woman's Christian Association hospitals; died Jan. 16, aged 76.

Gosnell, Thomas E. Ⓜ Louisville, Ky.; University of Louisville Medical Department, 1886; died Jan. 7, aged 99.

Graves, Stephen Monroe Ⓜ Clarksville, Ark.; (licensed in Arkansas in 1903); died Feb. 1, aged 88.

Greene, Garland Vestal, Mocksville, N. C.; North Carolina Medical College, Charlotte, 1916; veteran of World War I; served as county coroner; died Jan. 27, aged 68.

Gross, Leroy Calderwood Ⓜ Auburn, Maine; Tufts College Medical School, Boston, 1930; on the staffs of the St. Mary's General Hospital and the Central Maine General Hospital in Lewiston, where he died Jan. 23, aged 60.

Hancock, Virgil Kinney Ⓜ Seattle; Northwestern University Medical School, Chicago, 1919; veteran of World War I; died in the Swedish Hospital Jan. 13, aged 68.

Handelman, Milton S. Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1933; associated with Weiss Memorial and Mount Sinai hospitals; died in Hollywood, Fla., Feb. 5, aged 51.

Hane, Richard Lincoln Ⓜ Pacific Grove, Calif.; Ohio State University College of Medicine, Columbus, 1924; fellow of the American College of Surgeons; past-president of the Monterey County Medical Society and the Monterey Academy of Medicine; formerly practiced in Fort Wayne, Ind., serving as president of the Allen County Medical Society and as secretary of the Fort Wayne Medical Society; veteran of World War II; formerly held a fellowship at the Mayo Clinic in Rochester, Minn.; associated with the Peninsula Community Hospital in Carmel and the Monterey Hospital, where he died Jan. 25, aged 58.

Hanson, Adolph Melanchton Ⓜ Faribault, Minn.; born in St. Paul Sept. 11, 1888; Northwestern University Medical School, Chicago, 1911; member of the Central Society for Clinical Research; past-vice-president of the Minnesota State Medical Association, which in 1933 awarded him a gold medal in recognition of his isolation of the parathyroid hormone; in December, 1932, the U. S. Patent Office confirmed Dr. Hanson's claim to the discovery; Dr. Hanson made the Smithsonian Institution, Washington, D. C., the benefactor of all royalties for the furtherance of scientific research; in 1927 awarded the first prize for work on parathyroid gland by the Minnesota Society of Internal Medicine; in 1935 awarded the gold medal of the Southern Minnesota Medical Association for his exhibit at the state meeting; the following year named an associate in research of the Philadelphia Institute for Medical Research; veteran of World Wars I and II; on the staff of St. Lucas Hospital; inventor of dural separator and bone elevator used in brain surgery; for many years in charge of the Hanson Research Laboratory and donated its scientific equipment to the chemistry department of St. Olaf College in Northfield, July, 1942, to be perpetuated as a special laboratory for advanced students; in 1943 St. Olaf College conferred on him the honorary degree of doctor of science in recognition of his work on the isolation of the active principle of various hormones; author of "Practical Helps in the Study and Treatment of Head Injuries," 1925; also wrote a chapter, Management of Gunshot Wounds of the Head and Spine, in Volume XI, the Medical Department of the U. S. Army in the World War; contributor of numerous articles on parathyroid and thymus glands, head, spine, and superficial nerve surgery; died Jan. 15, aged 70.

Haworth, Edgar Sylvester Ⓜ Wichita, Kan.; Kansas City (Mo.) Hahnemann Medical College, 1907; died Jan. 9, aged 78.

Heaps, Carrie Erdman, Shamokin, Pa.; Woman's Medical College of Baltimore, 1907; died in the Shamokin State Hospital Jan. 5, aged 75.

Heine, William Howard Ⓜ Fremont, Neb.; University of Nebraska College of Medicine, Omaha, 1905; also a pharmacist; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; served during World War I; on the staff of the Dodge County Community Hospital; died Jan. 24, aged 81.

Hetrick, Llewellyn Evans, Hampton, Conn.; born in Lancaster, Pa., Dec. 11, 1875; Hahnemann Medical College and Hospital, Philadelphia, 1898; specialist certified by the American Board of Otolaryngology; life member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; member of the New York Academy of Medicine; formerly associated with the New York Medical College, Flower and Fifth Avenue Hospitals and the New York Polyclinic Medical School and Hospital in New

York City, where he served on the staffs of the Metropolitan and Flower and Fifth Avenue hospitals; veteran of World War I; following the war, was active for 22 years in the medical officers reserve corps, with the rank of colonel, and was retired in 1955, according to Army regulations; during World War II was active as examining physician in the Selective Service System; died in Colchester Jan. 20, aged 83.

Hilldrup, Don Guernsey Ⓜ Colonel, U. S. Army, retired, Indianapolis; born in Windfall, Ind., Nov. 9, 1887; Indiana University School of Medicine, Indianapolis, 1915; after serving an internship at the Indianapolis City Hospital, entered the medical corps of the U. S. Army in 1917 and served with both the American Expeditionary Forces and the Army of Occupation in Germany until 1920; later served at various Army posts; during World War II established military hospitals in Central Africa and later was surgeon of the Fifth and Sixth U. S. Army Service Commands; awarded the Legion of Merit; retired Aug. 31, 1948; at one time a member of the Army Medical Retirement Board in Washington, D. C.; served for three years as medical director of the Indianapolis American Red Cross Blood Bank; fellow of the American College of Surgeons; died in the Memorial Clinic of Indianapolis Jan. 28, aged 71.

Hine, Ulis Bryan Ⓜ Indianapolis; Indiana University School of Medicine, Indianapolis, 1925; served as Marion County deputy coroner and member of the medical staff of the Indianapolis Motor Speedway; associated with the Methodist and St. Francis hospitals, and the Community Hospital, where he died Jan. 26, aged 61.

Houloose, James Ⓜ Los Angeles; Rush Medical College, Chicago, 1920; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; for many years associated with the board of education of Long Beach; served with the Veterans Administration; died Jan. 11, aged 69.

Hubbard, Samuel Thatcher Sr. Ⓜ Hackensack, N. J.; University of Vermont College of Medicine, Burlington, 1907; specialist certified by the American Board of Ophthalmology; at one time secretary of the Bergen County Medical Society; on the staffs of the Holy Name Hospital in Teaneck and the Hackensack Hospital; died in the Veterans Administration Hospital, New York City, Dec. 23, aged 77.

Ives, Grace D. Ⓜ Great Barrington, Mass.; Woman's Medical College of the New York Infirmary for Women and Children, New York City, 1897; died Nov. 21, aged 97.

James, Theodoric V., Columbus, Miss.; Meharry Medical College, Nashville, Tenn., 1899; died in the Doster Hospital Jan. 15, aged 86.

Jefferson, James J., Johnstown, Pa.; born in 1874; Jefferson Medical College of Philadelphia, 1904; past-president of the Cambria County Medical Society, which in July, 1955, honored him for 50 years spent in the medical profession; at that time also was presented a plaque from the Medical Society of the State of Pennsylvania commemorating his long service as a physician; fellow of the American College of Surgeons; formerly surgeon of the Johnstown Plant, Bethlehem Steel Company, and Johnstown Works, U. S. Steel Corporation; for many years on the staff of the Conemaugh Valley Memorial Hospital; where he died Jan. 23, aged 84.

Johnson, Arthur Waldren Ⓜ Hales Corners, Wis.; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1914; served overseas with the Canadian Army during World War I; fellow of the American College of Surgeons; associated with the Columbia Hospital and the Milwaukee Hospital, where he died Jan. 23, aged 69.

Jones, Ralph Roy Ⓜ Winchester, Ill.; Barnes Medical College, St. Louis, 1905; served as president of the school board; associated with the Illini Community Hospital in Pittsfield; died Dec. 14, aged 84.

Kapnick, Israel Ⓜ Providence, R. I.; Harvard Medical School Boston, 1938; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; a cancer consultant to the state department of health; associated with the Charles V. Chapin Hospital, Miriam Hospital, and the Roger Williams General Hospital; died in the Rhode Island Hospital Jan. 3, aged 45.

Kelly Leo Joseph, Ⓜ Trenton, N. J.; Georgetown University School of Medicine, Washington, D. C., 1935; certified by the National Board of Medical Examiners; served an internship at the St. Francis Hospital in Trenton and Fitzgerald–Mercy Hospital in Darby, Pa.; veteran of World War II; associated with the Wills Eye Hospital and the Philadelphia General Hospital in Philadelphia; died in Yardley, Pa., Jan. 30, aged 50.

King, William Franklin Ⓜ Indianapolis; Ohio Medical University, Columbus, 1898; for many years state health commissioner and secretary of the state board of health, and head of the first division of adult hygiene and geriatrics; a member of the planning committee of President Hoover's White House Conference on Child Health and Protection; wrote the constitution for the National Association of Nursing Homes and last year received a plaque citing his service; past-president of the Indianapolis and state Exchange clubs; died in the Methodist Hospital Jan. 27, aged 84.

Kinnaird, Virgil Gibney Ⓜ Lancaster, Ky.; born in Lancaster Oct. 16, 1890; Jefferson Medical College of Philadelphia, 1913; served as councilor of the Seventh District of the Kentucky State Medical Association; member of the American Academy of General Practice; served overseas during World War I; honored by the Lancaster Junior Chamber of Commerce when he was designated as the "Outstanding Citizen of the Year"; past-president of the Garrard County Medical Society; past-president of the Lancaster Rotary Club; a director of the Centre College of Kentucky in Danville, where he served as a trustee for Kentucky School for the Deaf; served as chief of staff of the Garrard County Memorial Hospital; associated with the Ephraim McDowell Memorial Hospital in Danville; died Jan. 11, aged 68.

Kline, Samuel Ⓜ Sioux City, Iowa; Sioux City College of Medicine, 1908; served on the faculty of his alma mater; associated with the St. Joseph Mercy, St. Vincent's and Lutheran hospitals; died Jan. 22, aged 76.

Knight, Robert, Seneca Falls, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1902; veteran of World War I; health officer for the town of Seneca Falls and outlying districts, a position which he held for more than 30 years; formerly associated with the New York State Department of Health in Albany; on the staff of the Seneca Falls Hospital; died in Clifton Springs Jan. 12, aged 79.

Lamar, Richard Vanderhorst, Marietta, Ga.; University of Georgia Medical Department, Augusta, 1902; at one time on the faculty of his alma mater; formerly associated with the Rockefeller Institute in New York City; served on the staff of the Milledgeville (Ga.) State Hospital; died Jan. 22, aged 75.

Lawler, Edmund Griffin Ⓜ Chicago; Loyola University School of Medicine, Chicago, 1925; assistant clinical professor of pediatrics at his alma mater; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; chairman of the department of pediatrics at the Little Company of Mary Hospital, where he died Jan. 23, aged 59.

Lawrance, Jackson Stuart Ⓜ Reading, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1905; fellow of the American College of Surgeons; in January, 1956, was honored by the Berks County Medical Society for 50 years of practice and was given a plaque; veteran of World War I and was awarded the Distinguished Service Cross; served on the staff of St. Mary's Hospital in Philadelphia; associated with St. Joseph's Hospital, where he died Feb. 6, aged 78.

Leader, Pauline Marie, Lancaster, Wis.; State University of Iowa College of Medicine, Iowa City, 1894; for many years associated with the Clarinda (Iowa) State Hospital; died Feb. 7, aged 101.

Leet, H. Halbert Ⓜ Lexington, Ky.; born in Lexington March 5, 1911; University of Louisville School of Medicine, 1937; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology and the American Psychiatric Association; veteran of World War II; assistant professor of industrial medicine at the University of Cincinnati College of Medicine; instructor of neuropsychiatry at the State University of Iowa College of Medicine in Iowa City from 1939 to 1941; assistant professor of psychiatry at the Graduate School of Social Work, University of Kentucky, 1941-1942; lecturer of neuropsychiatry and psychosomatic medicine, Graduate School of Social Work, Tulane University in New Orleans from 1943 to 1946; associated with St. Joseph, Good Samaritan, Central Baptist, and Our Lady of the Oaks hospitals; died Jan. 26, aged 47.

Leymeister, Martin L. Ⓜ Reading, Pa.; Jefferson Medical College of Philadelphia, 1935; interned at the Wilkes-Barre (Pa.) General Hospital; member of the American Academy of General Practice; past-president of the Berks County Medical Society; served in the medical reserve corps of the U. S. Army from July 1, 1953, to July 31, 1955; associated with the Community General Hospital, where he died Jan. 25, aged 49.

Lieberman, Louis Manuel Ⓜ Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1930; veteran of World War II; associated with the Hospital of the University of Pennsylvania; died in Merion Station, Pa., Jan. 19, aged 54.

Linton, Charles Damon Ⓜ Walkerton, Ind.; Indiana University School of Medicine, Indianapolis, 1929; associated with the Holy Family Hospital, La Porte; died Dec. 30, aged 54.

Littlefield, Jesse Braxton Ⓜ Tucson, Ariz.; University of Texas School of Medicine, Galveston, 1922; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World Wars I and II; on the staffs of St. Mary's Hospital, Pima County General Hospital, and the Tucson Medical Center; consultant, Southern Pacific and Veterans Administration hospitals, and the U. S. Air Force Station Hospital, Davis-Monthan Air Force Base; died Jan. 12, aged 60.

Lockman, William L., Dallas, Texas; Memphis (Tenn.) Hospital Medical College, 1909; served with the Indian Service; died Jan. 10, aged 79.

Lyon, Edward George Ⓜ Dallas, Texas; Memphis (Tenn.) Hospital Medical College, 1911; served as full-time assistant health officer of the city of Dallas; died in the Veterans Administration Hospital Jan. 4, aged 74.

McAdams, Peter Stevens Ⓜ Cambridge, Mass.; Harvard Medical School, Boston, 1899; associated with the St. Elizabeth's Hospital in Boston, where he died Jan. 23, aged 86.

McCracken, Arthur James Ⓜ Bellefontaine, Ohio; Medical College of Indiana, Indianapolis, 1901; veteran of World War I; for many years city health commissioner and county coroner; died in the Monmouth (Ill.) Hospital Jan. 31, aged 85.

Marcy, Charles Howard Ⓜ Allison Park, Pa.; born in Cambridge Springs March 16, 1889; University of Pittsburgh School of Medicine, 1914; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians, American Trudeau Society, and the American Clinical and Climatological Association; fellow of the American College of Physicians, of which he was ex-governor; clinical professor of medicine at his alma mater; lecturer, University of Pittsburgh Graduate School of Public Health; past-president and secretary of the Pennsylvania Tuberculosis Society; medical director of the Tuberculosis League of Pittsburgh; veteran of World War I; member of the consultant staff, Presbyterian and Woman's hospitals, and Pittsburgh Diagnostic Clinic; member of the senior staff, Columbia Hospital in Wilkinsburg and St. Francis Hospital; area consultant in tuberculosis of the Veterans Administration; medical adviser, Industrial Hygiene Foundation; died in the Allegheny General Hospital, Pittsburgh, Jan. 18, aged 69.

Martin, Dwight Clifford, Summit, N. J.; Harvard Medical School, Boston, 1903; formerly chief of the bureau of tuberculosis, New York City Health Department; served on the faculty of Fordham University School of Medicine in New York City; formerly on the staffs of the Municipal Sanatorium of the Department of Health, Otisville, Seton Hospital, where he was president of the medical board, Bellevue, Presbyterian, and Knickerbocker hospitals; died Feb. 4, aged 80.

Martin, Hallie Eugene, La Fayette, Ky.; St. Louis College of Physicians and Surgeons, 1918; died in Hopkinsville Jan. 18, aged 73.

Masters, Howard Russell Ⓜ Richmond, Va.; born in Fredericksburg, July 2, 1894; Medical College of Virginia, Richmond, 1919; associate professor of clinical psychiatry and neurology at the Medical College of Virginia, where he joined the faculty in 1919; lecturer of abnormal and normal psychology at the College of William and Mary, Richmond division, from 1927 to 1929 and lecturer in psychiatry from 1927 to 1932; specialist certified by the American Board of Psychiatry and Neurology; past-president of the Tri-State Medical Association of the Carolinas and Virginia Neuropsychiatric Association, and the Mental Hygiene Society of Virginia, which he helped organize; member of the Endocrine Society, Richmond Academy of Medicine, and the American Psychiatric Association; a member of the Kappa Sigma, Omicron Delta Kappa, and Phi Chi fraternities; since 1926 member of the governor's advisory board on mental hygiene, Richmond; veteran of World War I; past-president and vice-president of the Memorial Guidance Clinic, and a member of its board since 1933; in 1953 appointed to the college of electors for the Hall of Fame of Great Americans; psychiatrist for the Virginia State Penitentiary from 1927 to 1930; associated with the Tucker Hospital, where he was president, Johnston–Willis, Sheltering Arms and Crippled Children's hospitals, and the Medical College of Virginia, Hospital Division; past-president of the Randolph–Macon Alumni Association; in 1956 the Randolph–Macon College awarded him an honorary L.L.D. degree; died Jan. 27, aged 64.

Meyerding, Edward August Ⓜ St. Paul; born in St. Paul Dec. 25, 1879; University of Minnesota College of Medicine and Surgery, Minneapolis, 1902; served as director of the division of hygiene and special classes of the public schools of St. Paul for fifteen years; for many years an executive secretary of the Minnesota Public Health Association and secretary of the Minnesota State Medical Association; on June 30, 1938, at the annual banquet of the state association, was presented with the society's first Distinguished Service Award created by its house of delegates, to be presented on occasion in recognition of special service to the association; past-president of the Mississippi Valley Conference on Tuberculosis; member of the House of Delegates of the American Medical Association from 1935 to 1936 and in 1939; in 1956 received the William G. Anderson Service Award of the American Association for Health, Physical Education and Recreation for his work with Minnesota school children; served during World War I and later was promoted to the rank of colonel in the reserve; organizer of the Minnesota Trudeau Society; member of the American College of Chest Physicians and the American Trudeau Society; died in St. Luke's Hospital Jan. 23, aged 79.

Mikolanda, Otto, Lorain, Ohio; University of Wooster Medical Department, Cleveland, 1903; for many years police surgeon; veteran of World War I; died in Millersburg Jan. 5, aged 78.

FOREIGN LETTERS

AUSTRIA

New Uses for Iproniazid.—At the meeting of the Society of Physicians in Vienna on Jan. 23, Dr. A. Pletscher stated that iproniazid inhibits the enzyme, monoamino oxidase (MAO), which is important in the decomposition of such monoamines as 5-hydroxy tryptamine (5HT) and pyrocatechol (CA). MAO-inhibitors of the hydrazine type (including iproniazid) which produce a long lasting effect are characterized by (1) a long-lasting increase of 5HT and CA in various organs (brain, heart, blood, and intestine); (2) an increase of 3-0-methyl levarterenol in the brain and a decrease of 5-hydroxy indoleacetic acid excretion as well as 3-methoxy-4-methoxy mandelic acid excretion in the urine; (3) increase in the rise of 5HT and CA, respectively, in the brain, depending on 5-hydroxy tryptophan (5HTPN) and dihydroxyphenylalanine (DOPA); (4) intensification of the central pharmacological effect of 5HTPN and DOPA (excitement and hyperthermy); and (5) antagonism against the reserpine-conditioned decrease of 5HT and CA in the brain, as well as against various pharmacological effects of reserpine on the central nervous system. It is probable that the clinical effects of iproniazid and its related compounds are partly based on MAO-inhibition too.

Dr. J. L. Rivier reported on 75 patients with angina pectoris who had been treated with iproniazid for 5 to 14 months. The initial dose was 50 mg. a day. The dose was increased every three to four days by 25 mg. to a maximum of 150 mg. a day. The effective dose was often found to be 75 to 100 mg. a day. In 50% of the patients pain subsided entirely; 25% of the patients were much improved; 16% were not improved; and 9%, all of whom had old and severe coronary lesions, died during treatment. A toxic effect of iproniazid should be excluded in these cases of death. The possibility of an orthostatic hypotension which can be elicited by iproniazid and might present a danger, at least theoretically, should always be considered. For this reason it was suggested that all patients be examined regularly and that the doses be increased gradually. Twenty-two patients with anginal pain on exertion were able to increase their physical activity with comfort during treatment and their electrocardiograms did not show any exacerbation.

Dr. H. Fleischhacker reported on 18 selected patients with angina pectoris who were given iproniazid. His results confirmed those of the previous speaker. The preparation proved to be effective only in patients with unequivocal typical attacks of angina pectoris based on severe coronary sclerosis. In others only moderate improvement was noted. Subjective cardiac complaints and sequelae of decompensation were not improved. In no case was a change of the electrocardiogram during or after treatment observed. Cardiac and other necessary treatments were given as indicated. The known side-effects were not observed in these patients. This was attributed to the fact that initial doses of only 25 mg. were given and that the dose was increased gradually to 25 mg. three or four times a day. The patients usually took this treatment for three to five weeks, the longest treatment being for four months, during which time the patient received 50 mg. daily. Special consideration was given to the evaluation of injurious effects of iproniazid on the liver. Results obtained from the serum lability test and from palpation were closely observed and in 12 patients liver biopsy specimens were examined. No evidence of liver damage was observed.

Dr. O. Zimmermann-Meinzingen gave iproniazid to 16 patients whose anginal pain was refractory to other forms of treatment. A detailed report was given on 10 of these patients whose treatment had been terminated. Of five of these whose angina pectoris was caused by coronary sclerosis two showed good improvement, two moderate improvement, and one no improvement. Two of these 10 patients had persistent angina pectoris after infarction, 1 of whom showed good improvement and 1 moderate improvement. Two others had persistent angina pectoris in the course of infarct formation, of whom one showed good improvement and one moderate improvement; and one patient who had coronary and valvular mesaortitis showed no improvement. These results were considered most encouraging and persisted after discontinuation of the other therapy aimed at dilation of the coronary vessels. A lasting favorable effect also persisted after iproniazid was discontinued. When last seen these patients were getting along well with small doses of vasodilators. No unfavorable circulatory changes were observed in those who were confined to bed. The blood pressure was not affected.

Dr. H. Walter-Büel of Münsingen reported on the use of iproniazid in the treatment of the psychoses, the treatment of which has changed greatly

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The items in these letters are contributed by regular correspondents in the various foreign countries.

since the introduction of chlorpromazine and reserpine in 1952. This change of treatment was concerned primarily with schizophrenic and organic psychoses. In the treatment of depressive states a similar change is now taking place with the use of iproniazid and imipramine. The speaker had used these preparations on more than 200 patients. Favorable results were obtained with iproniazid in 65% of those with menopausal, involutional, fixed psychoreactive, asthenic, and hypochondriac depressions. The drug was only slightly effective in patients with schizophrenia if they did not show a depressive component. Some loosening of the patient's frame of mind with increased activity became notable occasionally after several days, and more frequently after three to four weeks. This was often associated, although not strictly correlated, with an increase in appetite and body weight. Undesirable side-effects included vertigo, nausea, tendency to collapse, constipation, disturbances of sleep, occasionally disturbances of micturition and potency, and hyperreflexia. With a gradually increased dosage, not exceeding a daily dose of 150 mg., these side-effects remained mild. A comparison of iproniazid with imipramine is not easy. One or the other may be more effective in a single case, the factors of which are often complex. Supervision of the treatment by the physician is indispensable in view of the danger of suicide and because of the side-effects.

Dr. C. G. Tauber of Bern, Switzerland, reported on a series of more than 300 psychiatric patients, 134 of whom had been treated with iproniazid for 6 to 18 months. The drug was highly effective in 65% of those with depressive states of various origin. The best results were obtained in patients with endogenous depression, 85% of whom showed improvement. In many patients iproniazid therapy may be an adequate substitute for electroshock therapy and is not as frequently followed by recurrence as electroshock therapy. In about 10% of the patients, too early withdrawal of the drug was necessary because of a tendency to collapse or too strong a psychic action. About 10% of the patients were therapeutic failures. With a maximal daily dose of 150 mg. and with careful adaptation of the dosage, the side-effects were controllable or could be compensated by the administration of other drugs with a symptomatic action. Severe accidents, such as liver damage, did not occur among the 300 patients. The duration of treatment varied from three weeks to over nine months. Careful establishment of indications is indispensable for ambulatory treatment with iproniazid (all agitated patients are excluded) and so is continued supervision. Psychotherapeutic care and guidance is also important. New drugs with an analogous action are being developed.

Dr. V. E. Frankl reported that a woman with a phobic condition, who was undergoing psychotherapy, returned one day and stated that psychotherapy was no longer necessary since suddenly she had become free of fear and that this happened when she had to take iproniazid for tuberculosis. Since then he has treated 18 psychiatric patients with iproniazid, some of whom had been under observation for many years. In one of these patients the effect of the drug could be compared only with the therapeutic effect resulting from electroshock which the patient had been given several years previously. A woman with a compulsion neurosis of long standing, after taking iproniazid, described the characteristic effect of a so-called pharmacological leukotomy, which is known to result from the administration of certain tranquilizers or from such adrenergic agents as amphetamine. In this patient the effect of the pharmacological leukotomy was far superior to that of a surgical bilateral leukotomy which the patient had undergone earlier.

BRAZIL

Bleeding Time.—Dr. Cecy Barros and co-workers at the Hospital das Clinicas in São Paulo found that between the fingers and the lobes of the ears there is a significant difference in bleeding time, but there is no difference between the right and the left side of the body. On different days, in the same person, the bleeding time may show a significant difference. The mean bleeding time, in 100 normal subjects, was 1.75 (± 0.27) minutes. The bleeding time when prolonged, in almost every instance, indicated platelet deficiency. There were cases, on the other hand, with platelet deficiency and normal bleeding time, and some with a normal platelet count and prolonged bleeding time. The bleeding time, by itself, is not an index of the hemostatic capacity of the vascular and blood systems. In addition one needs a platelet count, a tourniquet test for vascular fragility, and other tests.

Uterine Rupture After Cesarean Section.—Drs. Antônio Guariento and co-workers at the Hospital Leonor Mendes de Barros in São Paulo studied a series of 855 patients who had had a previous cesarean section; 341 of them had a total of 401 iterative cesarean sections and the remaining 514 had 744 vaginal deliveries. In this entire series 30 uterine ruptures occurred in and 6 outside the hospital. In 9 of the 36 the scar was that of a classical cesarean section, and in 27 of a section in the inferior segment of the uterus. In 10 patients the rupture was diagnosed and a laparotomy was promptly performed. The classical symptoms and signs are often absent, and the diagnosis is sometimes made only during another cesarean section or by examination of the cavity after a vaginal delivery. The presence of meconium in a bloody urine indicates uterine rupture complicated by injury to the bladder. In spite of blood transfusion, improved anesthesia, and antibiotics, uterine rupture is still a serious threat to both mother and child. In this series there was one maternal death, in the third day of puerperium, and 15 fetal deaths. Conservative surgical measures such as hysterorrhaphy should be used whenever possible. If conditions do not allow it, a subtotal hysterectomy best serves the interests of the mother. The authors performed 31 hysterorrhaphies and 5 subtotal hysterectomies. They do not favor routine sterilization but treat each case on its merits.

CANADA

Society for Clinical Investigation.—At the annual meeting of the Canadian Society for Clinical Investigation in Vancouver, British Columbia, D. M. McLean of Toronto pointed out that few of the so-called nonparalytic cases of poliomyelitis in that area had been associated with poliovirus. In 1958 a common finding in children with aseptic meningitis in Toronto had been the isolation of Coxsackie virus B5 from feces samples. Enterovirus infection had also been responsible recently for a wider variety of syndromes, including pericarditis but not isolated myocarditis as found in southern United States.

D. Fraser of Toronto had studied two children with hypophosphatemic–vitamin D refractory rickets and found nothing wrong with the renal tubules. He thought that the excessive renal clearance of phosphorus was the result of secondary hyperparathyroidism, possibly due to defective intestinal absorption of calcium. D. McPherson of Vancouver had performed calcium infusion studies on normal subjects and patients with osteitis deformans and suggested that the labile storage pool of calcium in the skeleton was abnormally large in this disease with a faster bone blood flow of calcium.

P. Constantinides of Vancouver described a sulfated polysaccharide, known as Paritol-C, as a promising agent for the control of hyperlipemia. Given intravenously in nine patients with hypercholesteremia and hyperlipemia, it normalized the serum lipid levels in eight and the serum cholesterol levels in five, and resulted in clinical improvement. E. McGarry of Montreal had produced antibodies to anterior pituitary hormones in animals and found on immunochemical evidence that porcine, human, and bovine growth hormones were species-specific. Such antigen-antibody systems could be used to measure the levels of anterior pituitary hormones in body fluids. E. H. Venning of Montreal measured in vitro secretion of steroids from adrenal glands obtained from patients with pituitary basophilism or virilization. Adrenals from patients with virilization secreted less hydrocortisone and cortisone than did those from patients with pituitary basophilism, and there seemed to be an increased production of 17-ketosteroids in the virilizing syndrome.

J. C. Laidlaw of Toronto described experiments designed to relate findings of changes in steroid secretion during pregnancy with sex-hormone changes. Women with adrenocortical hypofunction who were taking hydrocortisone were given estrogen and progesterone. Estrogen administration produced no increase in hydrocortisone secretion in these, or in normal subjects who were given ACTH, but caused the same changes in metabolism of the steroid as occur in pregnancy. Progesterone did not cause these changes, and it was concluded that the alterations in hydrocortisone disposition in pregnancy are largely due to increased estrogen secretion. W. I. Morse of Halifax, Nova Scotia, showed that whereas oral tolerance of glucose was impaired in obesity of long standing, there was no difference between obese and normal subjects as regards intravenous glucose tolerance. The abnormal results in the oral test were not due to impaired glucose removal. R. A. Palmer of Vancouver made a plea for rectal administration of carboxylic acid resins in the control of hyperkalemia. In 17 patients with acute or chronic renal failure 25 Gm. of the resin mixture given by high enema at 4-hour to 12-hour intervals proved an efficient method of removing potassium. H. Cross of Kingston, Ontario, gave large rapid infusions of magnesium sulfate to hypertensive and normal subjects, noting a drop in blood pressure in the hypertensive but not in the normal subjects and an increased urinary excretion of calcium, sodium, and chloride ions but no change in phosphorus excretion. The hypertensive subjects showed increased excretion of potassium and increased glomerular flow rate and renal plasma flow. A. S. V. Burgen of Montreal followed the fate of intravenously injected radiomagnesium in the body. A rapid urinary excretion gave place to a slower one, with a total turnover time of 115 minutes. The site of the rapidly exchangeable magnesium is unknown, but the slowly exchangeable magnesium must be in skeletal muscle or bone. Serum magnesium was a poor indicator of the 24-hour exchangeable magnesium.

College of Physicians and Surgeons.—At the 28th annual meeting of the Royal College of Physicians and Surgeons of Canada in Vancouver, British Columbia, N. M. Lefcoe of London, Ontario, demonstrated a high degree of correlation between the timed vital capacity in patients with chest disease and the radiologist's assessment of the presence of emphysema, but the presence of a contracting lung lesion destroyed the correlation. E. R. Yendt of Toronto discussed the diagnosis and treatment of

20 patients with renal hypertension, and stressed the value of differential tests of renal function in diagnosis. In essential hypertension there was less than 10% difference in the volume and sodium concentration of urine secreted by the two kidneys, whereas in renal arterial disease the volume showed 50% difference and the sodium concentration 15%. A. E. Thomson of Winnipeg, Manitoba, stressed two problems in the treatment of acute renal failure: (1) use of adrenergic blocking agents to overcome peripheral vasoconstriction (he had used phenoxybenzamine at the onset with success); and (2) the difficulty of dealing with potassium intoxication, particularly as seen in traumatically injured patients. R. C. Dickson of Halifax, Nova Scotia, reported the successful use of potassium perchlorate as a thyroid depressant in hyperthyroidism and in euthyroid persons with angina pectoris. With a dosage of 200 mg. five times a day toxic effects were few. The drug was also of diagnostic value in struma lymphomatosa. H. McIntosh of Vancouver conducted a search for parathyroid tumors, particularly in patients with recurrent renal calculi, and recommended the intravenous infusion of calcium as a diagnostic aid. In the normal person the serum phosphorus level rises and the urinary phosphorus level falls, but in hyperthyroidism the serum phosphorus level does not rise.

J. A. Dauphinee of Toronto warned that hepatolenticular degeneration might be mistaken for paralysis agitans, and urged the examination of the eyes by slit lamp as a screening measure. In treating these patients penicillamine was more effective in removing copper than dimercaprol, but it might deplete the body of other trace elements. J. B. Dosseter of Montreal described the medical aspects of the first successful renal transplantation in Canada, performed on identical twins. Secretion of urine began almost as soon as the donor kidney had been sutured in place. Bilateral nephrectomy was performed five months later. Six weeks after the first operation the patient was ambulant and free from symptoms. P. Constantinides of Vancouver induced atheroma in rabbits by cholesterol feeding and showed that stilbestrol arrested the progress of the lesions, while vanadium and starvation had no effect, and linoleate had a partial effect. Stilbestrol caused toxic liver effects in half the rabbits. G. Monckton of Edmonton, Alberta, found in a patient with familial periodic paralysis that potassium was not stored in the liver as had been suggested by radioactive potassium studies but that before and during attacks of paralysis there was marked sodium retention with a drop in urinary sodium. A diet low in sodium controlled the paralysis.

W. Pisesky of Edmonton had found in experiments on rats that triethylene thiophosphoramide retarded wound healing, while norethandrolone counteracted this. K. S. Morton of Vancouver followed up 62 patients with traumatic dislocation of the hip and noted that the chief factors determining the result were severity of injury and delay in reduction. F. P. Dewar of Toronto analyzed 145 fractures of the carpal scaphoid and showed that, provided such a fracture was immobilized in plaster, it was difficult to prevent it from healing. Conservative treatment is the only acceptable one, even with missed fractures. T. K. Goodhand of Winnipeg had replaced an entire ureter in dogs with an ileal loop, removed the contralateral kidney, and killed the animals 4 to 12 months later. The isolated loop was a satisfactory substitute for the ureter, and it seemed better to replace all rather than part of the latter. The blood urea level soon returned to normal and chloride reabsorption by the ileum was not a problem.

Vitamin C-Fortified Milk.—Last year a series of cases of infantile scurvy was reported from Toronto and Winnipeg. Medovy recommends (*Canad. M. A. J.* 80:213, 1959) that all evaporated milk be fortified with vitamin C in view of the decline in breast feeding, the reluctance of some mothers to give orange juice, and the general confusion in the lay mind about vitamin concentrates. One firm has produced a milk incorporating 75 mg. of ascorbic acid per 15-oz. can, and the product has been subjected to rigorous tests in the Winnipeg Children's Hospital without loss of vitamin C content. Two patients who had scurvy were treated solely by the fortified milk, with prompt clinical improvement supported by radiologic evidence.

Prepaid Optometry.—A complete plan for optometry on a prepaid basis has recently been started by the Canadian Association of Optometrists, which has organized a nationwide nonprofit organization called Canadian Optometric Services, Inc., operating under a government charter. Commercial, industrial, or professional groups can enroll, and services include examination, refraction, and provision of lenses and frames. The subscriber has a choice of optometrists. The cost of plans will vary depending on their type and extent of coverage, but a basic plan is expected to run at 65 to 80 cents per person per month.

Prescription Insurance.—Another experiment in prepaid care started in March, 1958, in Essex County, Ontario, when Prescription Services, Inc., began as the first known pharmaceutical prescription plan in Canada. It serves an area with a population of 200,000, and agreements with all but 7 of the 75 pharmacies involved have been signed. A progress report on the first six months shows that of 548 persons enrolled in the last month 104 had 211 prescriptions filled with an average ingredient cost of $1.86 and average retail price of $3.72. Organized labor has been favorable to the new plan, but management has been frank in its opposition to providing another fringe benefit for employees. Sponsors believe that the plan can succeed with slight modifications.

Schizophrenia.—Osmond and Hoffer recently reviewed research into the chemical nature of schizophrenia (*Canad. M. A. J.* 80:91, 1959). Steps in the studies included recognition of a relation between mescaline intoxication and acute schizophrenia; discovery of the relation between the chemical constitution of the former and that of epinephrine; reports by some asthmatics that when their epinephrine for self-administration turned pink they experienced hallucinations after its use; and the discovery that one of the products of pink epinephrine was adrenochrome, which in normal subjects produced schizophrenic sensations. Another breakdown product of epinephrine is adrenolutin, and either of these breakdown products may prove to be the naturally occurring mescaline-like substance responsible for the sensory changes in schizophrenia. It has also been shown that schizophrenics are less able to remove adrenochrome from the blood than are normal persons. It seems that d-lysergic acid (LSD-25) retards the destruction of adrenochrome and permits its accumulation in the body.

INDIA

Mongolism.—Dayal and Agarwal (*Indian Journal of Child Health*, vol. 7, December, 1958) stated that mongolism is not so uncommon in this country as is usually believed. They observed 18 cases in children between 3 months and 11 years of age, all of whom showed microcephaly and brachycephaly. Thinning of the skull bones was evident in 12, and 2 also showed nonclosure of sutures. The fingers and toes showed the deformities commonly described, i. e., increased space between the first and second digits, short digits, and a short terminal phalanx of the fifth digit which was turned inward. The sole and palm creases showed deviations from normal in about half the patients. Macroglossia was a universal feature, the tongue showing fissures and conforming to the "scrotal type" in most patients, although in seven there were no fissures on the tongue. In 16 the ears were small and turned forward. An interventricular septal defect could be diagnosed clinically in only one patient. This was later confirmed by x-ray and electrocardiogram. The typical oblique palpebral fissures and epicanthic folds were present in all patients. In one the orbits were winged and obliquely set and one had nystagmus. Congenital cataract was present in two and strabismus was seen in one.

All the children showed severe mental retardation and the various milestones in the physical development were delayed. No correlation could be detected between parity, parental age, and idiocy, and there was no history of such maternal illnesses as mumps, influenza, or rubella in any of the cases. Consanguinity was found in one case only. Thus, in this study, late closure of fontanelles and persistence of frontal sutures was not a frequent finding as is commonly described and no widening of fissures and foramina could be demonstrated. No common etiological factors could be established.

Tetralogy of Fallot.—R. H. Betts and co-workers (*Indian Journal of Surgery*, vol. 20, December, 1958) stated that the clinical findings in patients with the tetralogy of Fallot are variable. The two dominant lesions are the pulmonic stenosis and the interventricular septal defect. The authors operated on 79 patients with this condition and 13 died. An autopsy was performed on 11, and it was concluded that such patients, operated on before the age of 3, suffer from an extreme degree of disability. The authors usually deferred the operation when there was a possibility that the child would live to the age of 3 or older. All risks are increased in infants and the death rate in children below 3 years of age in this study was 50% as compared to 12.5% for those above 3. Angiocardiography and cardiac catheterization were not usually performed on the severely incapacitated child under 3 years of age as they were believed to increase the risk. This measure may, however, be justifiable in some cases in order to determine the exact site of obstruction preoperatively so that the proper operation can be planned. This is especially important in children who are not good subjects for the Blalock operation due to a small subclavian artery, in which case a Pott's operation, if there is a left aortic arch, or a direct pulmonic valvotomy, if the obstruction is predominantly valvular, would be advisable. The pericardium was not opened routinely but the extent of the pulmonary stenosis was assessed by feeling for the cone of the pulmonary valve and the easily obliterated thrill through the intact pericardium.

The most frequent cause of death in this series was faulty postoperative management. Cerebral thrombosis is a common complication in deeply cyanotic patients and its risk increases if there is marked dehydration. This complication developed in four patients, two of whom died. Three other deaths were due to errors in management—one patient developed atelectasis of the left lung which progressed to early bronchopneumonia, another developed a severe diarrhea, and one had a persistent paralytic ileus. On the 5th postoperative day a laparotomy was performed on the last mentioned patient. No cause for the ileus was found. The gastric aspiration tube became blocked on the next day and a large amount of material was vomited. Some of it was aspirated and the child died soon after. In three of the fatal cases, there was an error in diagnosis. One child, less than 2 months of age, was believed to have tetralogy of Fallot and cerebral thrombosis. Pott's operation was performed but the child died after two weeks and at autopsy was found to have not a tetralogy but a transposition of great vessels with a small interventricular septal defect. The cerebral symptoms were due to the presence of a large porencephalic cyst which was the cause of death.

Another patient was found to have pulmonic stenosis only and should have had a valvotomy instead of a shunt operation. The third patient was diagnosed preoperatively as having pulmonic stenosis with an atrial septal defect. At operation he was thought to have both valvular and infundibular stenosis and a pulmonary valvotomy was performed. Autopsy showed that, instead of a pure pulmonic stenosis, the child had a tetralogy of Fallot with valvular and infundibular stenosis, an atrial septal defect, and a patent ductus arteriosus. In two patients errors in operative technique caused death. In one, a Blalock type of anastomosis was performed but was inadequate as the left pulmonary artery was extremely small and friable. The anastomosis was occluded by a thrombus. An anastomosis should have been done on the right side as the right pulmonary artery was of normal size. A preoperative angiocardiogram would have helped in this case. In the second case laceration of one of the cusps of the aortic valve was produced accidentally by the valvulotome and caused an aortic insufficiency which contributed to the patient's death.

Errors in choice of operation accounted for two deaths. One was thought to have a pure pulmonic stenosis and a valvotomy was performed, but he had a tetralogy of Fallot and should have had a shunt operation. Another was an infant of 7½ months and a Blalock operation was performed. The vessels were small and at postmortem the anastomosis was found to be completely occluded by a thrombus. The child also had a combination of valvular and infundibular stenosis and a valvotomy would have given him enough relief so that a shunt operation could be done when he was older. In two the cause of death could not be determined and associated defects probably contributed to the death of others. Thus one child of 7½ months had a right aortic arch and a marked dextroposition of the aorta. The second had an extreme dextroposition associated with a diminutive pulmonary artery. Two others had peculiar valve-like structures within the interventricular septal defects, causing obstruction to the blood flow and imposing an additional burden on the right ventricle.

National Register.—The government is compiling a national register of all qualified scientific and technical personnel of the country. The purpose of this register is to provide comprehensive and authoritative information on national resources of scientific and technical manpower; to serve as a clearing house for information on resources of and requirements for scientific and technical manpower; to develop a special section of the register to maintain current information on Indian nationals studying or working in technical fields in foreign countries; to provide information on persons having highly specialized training and experience, when an appointing authority finds it difficult to get suitable candidates to respond to public advertisements; and to assess the gaps in the training and utilization of scientists and technologists through technical manpower research. The National Register Unit prepares study reports based on the information contained in the register. The register lists those (1) holding at least a postgraduate degree in a science, (2) holding at least a bachelor's degree in agriculture, veterinary medicine, and other fields, (3) holding a degree in engineering and technology, and (4) who are medical specialists.

Hypothermia in Surgery.—Saini and Bett (*Indian Journal of Surgery*, vol. 20, December, 1958) used hypothermia of various degrees in 98 patients, cooling the skin surface by blankets. Of these, 66 had tetralogy of Fallot and hypothermia was used to improve the operative risk. Many were deeply cyanotic and many had rapid pulse rates. The range of temperature varied from 92 to 88 F. Six patients with pulmonary stenosis were also operated on under hypothermia. Hypothermia here was used as an adjunct, as it was also in another group of nine patients with acquired heart disease. The operative mortality under ordinary anesthesia is high in such cases; three of five patients with mitral stenosis were saved by operation under hypothermia. The remaining four had constrictive pericarditis and hypothermia helped to reduce the operative risk. Hypothermia was also used in operations where local occlusion of circulation was necessary. The total number of deaths in the whole series was 18, and of these 4 could be attributed to hypothermia. One patient with mitral stenosis developed ventricular fibrillation; cardiac arrest occurred in a patient with atrial septal defect; excessive bleeding from the surface of the heart led to death in a patient with constrictive pericarditis; and an apparently acidotic syndrome proved fatal in a patient with atrial septal defect.

Vasectomy for Sterilization.—Ohri and Jhaver (*Indian Journal of Surgery*, vol. 20, December, 1958) studied the changes in the testes of rats and men after vasectomy. The first 50 operations on human subjects were by the standard two-incision technique under local anesthesia. Later, one central scrotal incision was used, about 1 cm. in length, through which bilateral vasectomy was done. Patients were not admitted to hospital and contraceptives were advised for about six to eight weeks, after which the semen was examined for living spermatozoa. They were followed up for six months to four years.

Old male rats were used for the experimental study. They were divided into three groups. The testes were removed from the first group for histological examination. The second group served as controls, their testes being removed for study at the end of six months, and in the third group, vasectomy was performed and the rats subjected to orchiectomy at varying intervals. Study of the whole group covered about six months. The rats in the first and second group showed normal testicular tissue on histological examination with active spermatogenesis, thus showing absence of change in the second group due to age during the period of experiment. In the third group, within two weeks after the operation, the seminiferous tubules started showing degenerative changes associated with congestion of the stroma. The degenerative changes increased for the first eight weeks. Eight weeks after the operation, the appearance was striking, consisting of islands of normal seminiferous tubules surrounded by degenerated tubes and vice versa, representing active regeneration of a focal type. The interstitial tissue, from the 10th week on was more noticeable, its proliferation being marked toward the end of the experiment.

After vasectomy in men, 6 complained of diminution of sexual capacity, 86 noticed an increased sexual strength and desire, and 198 claimed that their sexual power remained unchanged. There was weight loss in 18 patients after operation, no change in weight in 160, and a gain in 112. Relief from the anxiety from further additions to the family was probably the cause of the pleasant mental reaction to the operation, which was in some cases associated with increased sexual capacity; 268 felt very happy after the operation. The reaction of the wives of these men varied; 96 felt happy because of freedom from further childbearing, 190 showed no particular reaction, and 4 reported conception after the operation. Failure of the operation in controlling conception was specially noticed in cases where plain catgut was used to ligate the two ends of the vas, rapid absorption of which probably allowed reestablishment of the lumen.

Viral Encephalitis.—Mathur and Prasad (*Journal of the Indian Medical Association*, vol. 32, Jan. 16, 1958) analyzed a series of 161 cases of viral encephalitis seen in an epidemic, July to September, 1958. The peak was reached between July 7 and 21. The largest number of deaths however were reported in the last week of September. Persons belonging to both upper and lower economic strata were affected. Often more than two members in the same family were attacked. There was no report of person-to-person transmission in the hospital wards. Most of the patients (89%) were below 8 years of age (range 1 month to 35 years). The onset was usually sudden, with restlessness, vomiting, diarrhea, and a temperature of 102 to 105 F (38.99 to 40.56 C). Convulsions and twitchings then appeared, the child talked incoherently or became delirious, and lapsed into semiconsciousness or unconsciousness. The fever was most commonly continuous or remittent but in some it was intermittent. It returned to normal by lysis. A secondary rise was seen in 15.5% of the patients after a complete remission lasting two to four days; 1.8% also showed a tertiary rise of temperature. Two patients showed blindness and one had dimness of vision. One had myoclonic movements and two developed tremors of a rhythmic Parkinsonian type which disappeared on recovery. Two patients showed spastic paraplegia at the onset and one had a flaccid paraplegia. Two had hemiparesis. None of these had any residual effects after recovery.

More than half the patients had nuchal rigidity with a positive Kernig's sign and 42.2% had an extensor plantar reflex. Pulmonary involvement was common and three patients died of acute pulmonary edema. Ophthalmoscopic examination in 60 patients revealed optic neuritis in 3 and pallor of the disks in 2. Clinically the patients could be divided into a fulminant (34.8%), moderate (33.5%), and mild (31.6%) type. More than 67% had polymorphonuclear leukocytosis. A low blood sugar level was found in only 15%. The cerebrospinal fluid was under increased pressure on lumbar puncture in 76%. The most common change was pleocytosis to the extent of 5 to 50 cells. In addition to symptomatic treatment, the patients were divided into seven groups and given different drugs (tetracycline, penicillin, chloramphenicol, ACTH, a combination of tetracycline and ACTH, ACTH with penicillin, and normal saline solution). The results with normal saline solution (given intramuscularly) and ACTH alone were the best. There were 45 deaths, giving a mortality of 27.9%. Among the 112 patients who were discharged as cured, 8 had a relapse. No residual effects were noted in about 70% of those who were discharged as cured and could be followed up for one to three months.

NORWAY

Iproniazid for Psychosis.—Haug and Kolstø (*Nord. med.* 60:1789-1794 [Dec. 11] 1958) treated 22 chronically psychotic male patients with iproniazid. Most of these patients were schizophrenics. All of them presented long-standing apathy and/or depression, with little or no variation in the clinical course of their illnesses. The patients were given 50 mg. of iproniazid three times a day for 10 weeks. Significant changes in behavior were observed in 16, and in 6 no changes were noted. With the exception of one patient who became more depressed, all showed a definite increase in the general activity level and an elevation of mood. From a practical clinical point of view, however, only 6 could be classified as improved; 10 became overtly aggressive and hyperactive to an extent that made them difficult to manage in the wards. In several, hallucinations were intensified. During the trial period, treatment was discontinued in 7 and the dosage reduced in 11 because of severe psychiatric and somatic complications. One patient was on the verge of delirium. One developed melena. Another, who had never shown signs of heart disease, died of myocardial infarction. Hypotension, dizziness, and fainting occurred in some. Hyperreflexia, constipation, and anemia were common but not severe. Chromatographic analysis of the spinal fluid of five patients showed an increase of the albumin fraction. The authors cautioned against uncritical use of iproniazid to activate chronically psychotic patients. The drugs tended to reactivate violent psychotic outbursts, repeating the acute early phases of the illness, and its use was complicated by widespread disturbing and dangerous somatic complications. Further study is needed before the usefulness of the drug in the treatment of chronic psychotic patients can be determined.

SWEDEN

Endocrinological Institute.—The only hospital department in Europe specializing in endocrinological research was inaugurated in January at the Stockholm Carolinian Hospital, under the chairmanship of Professor Rolf Luft. One half of the floor space is occupied by laboratories. The most important task of the new institute will be further research in endocrinology. Important projects include studies on diabetes, thyroid diseases, and hormone treatment of certain types of cancer.

Protons Used in Brain Surgery.—Proton rays were used in brain surgery at the Upsala University in December. Now the operation has been judged successful. The patient was a 55-year-old man suffering from chronic depression, and the operation was the result of close teamwork between neurosurgeon, histopathologist, radiologist, and the personnel of the synchrocyclotron department of the institute. Experiments with the use of a proton ray as a surgical instrument were first made at the University of California in Berkeley, where a different procedure from the one used at Upsala was followed. This operation, the first of its kind on a human being, was preceded by extensive animal experiments on mice, rabbits, and goats which were subjected to careful pathological examination in order to ascertain the possible aftereffects. The results were reassuring. Professor Lars Leksell, a neurosurgeon of Lund University, believes that the method will be specially useful for treatment of chronic pain, paralysis agitans, and certain psychic disorders.

The protons, with an effect of 190 million electron volts, cut off deep-lying nerve paths in the brain. The advantages over conventional brain operations is that this procedure diminishes the hazards and complications involved and shortens the time of recovery. The new type of operation is not painful and takes place without anesthetics. Hospitalization is not required. The Upsala patient was in touch with the operating team by means of a microphone, the operating crew watching the procedure by television in order to avoid being subjected to ionizing radiations. The treatment was interrupted about 40 times to change the angle of approach of the ray, and the patient was thus never alone more than about a minute at a time. Dr. Börje Larsson was the nuclear scientist responsible for the instruments used. The new method is not likely to be generally used for many years. Several such operations, however, have been planned.

UNITED KINGDOM

Reducing Tablets.—Drs. A. Foster and C. Seager of Barrow Gurney Hospital are compiling data for the Poisons Board on the use of reducing tablets, which they claim are producing drug addicts. Women pay an average of $1 weekly for the tablets, which are sold at the rate of one million a month. The Poisons Board is considering making a number of reducing preparations available only on prescription. A woman recently appeared before the courts accused of forging doctors' prescriptions to get reducing drugs, which she had been taking for five years. Her weight had dropped from 154 to 84 lb. (69.9 to 38.1 kg.), and she suffered from severe insomnia. She finally concluded that it was "better to stay fat and happy."

Electronic Pacemaker Sutured into the Heart.—One of the major hazards of open-heart operations for the closure of ventricular septal defects is damage to the conduction mechanism and consequent heart block. This has been dealt with by Ross and co-workers by direct stimulation of the ventricles by an electrode sewn into the heart and connected to a pacemaker (*Lancet* 1:392, 1959). A 7-year-old girl was operated on by Sir Russell Brock for closure of a ventricular septal defect. A complete cardiac bypass was maintained for just over 30 minutes, and the heart was arrested for this period with potassium citrate. The defect was closed, but shortly afterward fibrillation and finally heart block occurred. The bared ends of two electrodes, one acting as a stimulator and the other as a spare, were sutured with fine silk into the anterior surface of the right ventricle, about 2 cm. apart. An indifferent electrode was implanted into the right pectoralis major muscle. All three leads, which were 2-ft. lengths of plastic-covered six-strand fine wiring used in telephone equipment, were exteriorized by separate incisions and anchored to the skin. The ends were connected to a battery-operated artificial pacemaker adjusted to maintain a rate of 120 beats per minute, the usual postoperative rate of patients who undergo similar operations without developing heart block. The pacemaker, set to deliver 4 volts, which was just above the minimum voltage necessary to cause the heartbeats to follow the pacemaker consistently, accompanied the patient back to the ward. An electrocardiograph-monitoring oscilloscope was connected to the pacemaker.

The heart block and its management by the pacemaker was the only postoperative complication. On the second postoperative day the child suddenly became pulseless for 10 seconds, presumably due to cardiac arrest, but quickly recovered. The pacemaker was switched off on the fourth day and the heart maintained its own rate of 80 to 90 beats per minute until the eighth day, when it was necessary to use the pacemaker again. It was used intermittently until the 11th day. Then 5 mg. of isoproterenol was given orally three times daily, and the pacemaker was disconnected. The isoproterenol therapy was stopped 11 days later. On the 21st day, when it was evident that the heart was in spontaneous sinus rhythm, the electrodes were removed by slight traction. The girl was discharged a month later and was well when last seen.

New Type of Pneumoconiosis.—During a survey by the Pneumoconiosis Research unit of the Medical Research Council on random samples of men of known occupation, a new type of industrial pneumoconiosis was brought to light (*Tubercle* 39:399, 1958). The investigations included a detailed industrial history, measurement of the ¾-second forced expiratory volume (FEV 0.75), and a chest film. The films were read by experts without any knowledge of the occupational or medical history of the subjects. One occupational group, designed as a control for the industrial groups, consisted of men who, as far as was known, had not been exposed to dust or fumes likely to damage the lungs or cause pneumoconiosis. When the data for this group were tabulated, however, it was found that a few of the chest films showed evidence of pneumoconiosis. These were from men who had worked for 40 years or more on the footplate of a train as a driver or stoker. The FEV was above the average for men of similar age in such occupations as agriculture. Although there was no evidence of pulmonary disability, the chest films showed unmistakable signs of pneumoconiosis. It was therefore concluded that after 40 years of driving on the footplate of a train sufficient dust is retained by the lungs to be roentgenologically visible.

New Viruses.—During an outbreak of a respiratory illness resembling coryzal bronchitis in a residential nursery in Sheffield, Sutton and co-workers (*Lancet* 1:395, 1959) identified two new virus strains. Throat swabs from the children were inoculated into monkey-kidney tissue cultures. Hemagglutinins for chicken and human cells appeared in the mediums and two strains of virus, hitherto unreported in Europe although recently described in America, were identified. These strains, known as HA1 and HA2, belong to the myxovirus group. They were detected by the technique of hemadsorption.

Twin Pregnancy in a Double Uterus.—The extremely rare case of a twin pregnancy in a double uterus was reported by Dr. N. Kennedy, a general practitioner of Kent. Twins were diagnosed antenatally in a woman with two cervices who had had four previous pregnancies. She went into labor spontaneously at the expected time and after 12 hours was delivered of an asphyxiated infant who died shortly afterward. After delivery the right side of the mother's abdomen was seen to be empty and uterine contractions ceased. The remaining fetus lay obliquely with the vertex presenting high over the pelvic basin on the left. Three weeks later the second twin was born via the second cervix. A hysterosalpingogram taken subsequently revealed two uteri with separate cervices, the left larger than the right, showing that both uteri had been gravid. Several interesting points arise from this case: One uterus went into labor independently of the other; the right uterus retracted during the expulsion of the first twin, while the left uterus was undergoing first-stage contractions; and lactation was absent after the birth of the first twin but established itself shortly after that of the second.

Television Angina.—In a letter to the *British Medical Journal* Dr. G. Rose reported a new condition, observed at a clinic for coronary diseases, which he calls "television angina." This affected 20% of those patients with angina pectoris who watched television programs and was provoked by seeing violent incidents on the screen. Among those liable to emotionally produced attacks only a few could enjoy viewing television without cardiac pain. In some patients television angina was the only type of rest pain. Rose stated that commercials were innocuous, but Westerns and plays or films depicting violence or excitement often provoked anginal attacks.

Extravenous Injection Not Negligent.—Last June a judgment was given in favor of a patient who sued the North Liverpool Hospital Management Committee for negligence in the administration of thiopental for varicose vein operation. It was claimed that the thiopental, which should have been given intravenously, entered the surrounding tissues and produced an abscess. The case against the committee was that it was vicariously responsible for the negligence of the anesthetist. The judge awarded damages of $1,218. The case was taken to the court of appeal. The patient was an exceedingly fat woman; the anesthetist had inserted his needle obliquely over a vein and aspirated to make sure that the needle was in the vein. Blood entered the syringe, and he then injected 5 ml. of thiopental solution. As this produced no anesthetic effect, the needle was withdrawn. Further attempts were made in both arms to locate a vein but without success. It was assumed that the thiopental had entered the tissues and not the vein, particularly in view of the later development of an abscess.

One error alleged was that the anesthetist should have aspirated blood repeatedly into the syringe during the injection to make sure the needle remained in the vein, but the judge found in the anesthetist's favor on this point. The second error alleged was that he failed to ask the patient if she felt any pain. The fact was that she did not, nor was there any swelling at the time; so even if she had been asked she would have replied in the negative. The court of appeal decided that there was no evidence of negligence on the part of the anesthetist.

Improved Obstetric Care.—The committee set up in 1956 to review the organization of the maternity services of England and Wales (Ministry of Health Report of the Maternity Services Committee, Her Majesty's Stationery Office, 1959) reported that the care of a woman in pregnancy and childbirth is divided between the three separate parts of the National Health Service, namely, the hospitals, the general practitioners, and the local health authorities. In general the system works reasonably well, although overlapping and impairment of service are at times inevitable. The report recommends that in future only general practitioners who are qualified and experienced in obstetrics should be paid for maternity work. At present doctors on the obstetric list of the National Health Service receive $20.60 for the complete obstetric care of a patient. The fee is $15 for those not on the list. The committee recommends that only doctors on the obstetric list, of which there are 14,400, should receive payment for maternity work. It is suggested that in the future admission to this list should be more selective. A six-month obstetric internship is regarded as a minimum qualification, and to remain on the list a doctor should have conducted at least 60 obstetric cases in the preceding three years.

Obstetrics, formerly practiced by many general practitioners, has now become highly specialized. There are 737,704 births yearly in England and Wales, nearly 65% of which are in hospital. To remain competent a doctor should attend a minimum of 50 cases a year but, allowing for hospital births, there cannot be more than 12 or 13 cases for each practitioner and this is insufficient to maintain obstetric skill. The suggestion is therefore made that a higher standard should be required. Fewer doctors would then practice obstetrics, and those who did would treat more such patients than at present. Remuneration should be correspondingly higher. The report also advocates the supervision of maternity units staffed with general practitioners by specialized obstetricians, without their trespassing too closely on clinical freedom. This would be difficult to achieve and would probably be resented by general practitioners. Many women, particularly of the middle class, prefer to have their second babies delivered at home rather than in hospital.

Other recommendations made by the committee include the provision of sufficient hospital accommodation for 70% of all confinements and antenatal beds for 20 to 25% of these. As it costs the patient less in hospital than at home it is suggested that the mother confined at home should receive a maternity grant of about $14. The committee considers that obstetric care should still be under the tripartite administration of hospital, general practitioner, and local health authority. To unify it under a single authority would create more problems than it would solve, but it suggests that the general practitioner–obstetrician could eventually replace the local health authority's medical officer in providing antenatal and postnatal care. The expectant mother should be instructed in child care and hygiene and should be provided with a maternity aid service after the birth of the baby. There should be sufficient premature-baby units to give country-wide coverage, and enough obstetric "flying squads" to attend all emergencies that cannot wait for hospital care. Resuscitation equipment, which should be kept in all hospitals, should be available to general practitioner–obstetricians. The committee considers that these should have access to maternity beds in hospitals, although few do at present. A final suggestion is the introduction of a national "maternity card" on which the mother's complete obstetric history could be recorded.

Idiopathic Hypoproteinemia.—Generalized edema may sometimes occur as a result of alteration in the metabolism of plasma proteins, resulting in severe hypoproteinemia. The patient appears to eat and absorb protein, to synthesize albumin, and to show no evidence of protein loss. Gordon, Schwarz, and Jarnum, working independently, showed that in this condition, which is known as idiopathic or hypercatabolic hypoproteinemia, the proteins are lost from the gastrointestinal tract (*Lancet* 1:325, 327, 1959). These workers have succeeded in labeling polyvinylpyrrolidone (PVP) with radioactive iodine (I^{131}). This substance, with a molecular weight of 40,000, is unaffected by proteolytic enzymes, and is used as a plasma expander. PVP with I^{131} is useful for measuring the permeability of the alimentary tract to serum proteins. The fecal PVP–I^{131} content was measured after a single injection in 13 patients with idiopathic hypoproteinemia. In all of them there was excessive loss into the gastrointestinal tract, showing that in these patients there was an abnormal permeability of the tract to macromolecules. Albumin synthesis, in terms of the degradation of I^{131}-labeled albumin, was high in all cases, showing that the edema was not due to lowered blood albumin level. The edema would thus appear to be due to protein loss in the gastrointestinal tract. It is not known whether this is due to capillary leakage, a mucosal defect, or both.

CORRESPONDENCE

REMOVAL OF PLASTER CASTS USED IN WALKING

To the Editor:—For years my colleagues and I have been removing plaster casts used in walking by cutting them laterally or anteriorly. Recently, I came to the conclusion that it would be much easier to cut a cast posteriorly over the calf of the leg. This is the softest spot of the leg, and there is no bone anywhere near. This way one does not have to make the cut curving around the foot but merely cuts the plaster from the top to the heel. After having done that, all that is necessary is to spread the cast just enough to allow the patient to slip his foot out backwards. I have not found that method described in the literature and thought it might be of some help to others, as it was to me.

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CLONIC CONVULSIONS

To the Editor:—In the case report on "Clonic Convulsions After the Oral Use of Perphenazine (Trilafon)" in The Journal (169:834-835 [Feb. 21] 1959), the authors suggest that the patient had an epileptiform seizure. From the case summary it is noted that jaw and neck tremors were observed first, followed by generalized, clonic convulsions without loss of consciousness, opisthotonus, and rolling of the eyes upward. This description is reminiscent of the group of dyskinetic reactions of the extrapyramidal syndrome. Coming on shortly after the administration of perphenazine and characterized by tremors of the head and neck, hyperextension of the trunk, oculogyric crises, and generalized muscle spasms, it seems to be a striopallidal disorder rather than epilepsy.

These bizarre and sometimes frightening myoneural disturbances occasionally occur after the use of even small amounts of phenothiazines with a piperazine ring in the side chain and have been mistaken for epilepsy, encephalitis, and tetany. It would be rare for a generalized epileptic convulsion to occur without concomitant loss of consciousness. Freyhan recommends intravenously given caffeine and sodium benzoate, or phenobarbital sodium, during the acute phase. In addition, an anti-Parkinsonian agent should be given. When it is necessary to continue use of the drug, temporary reduction of dosage along with continued use of the anti-Parkinsonian compound is a relatively safe procedure. Apparently, physiological tolerance occurs and the dyskinetic syndrome is rarely seen after one week of phenothiazine therapy. Although this group of drugs may decrease the seizure threshold, this effect is considered a high dosage phenomenon. Epileptic convulsions would not be expected to occur on the first day of therapy.

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"LABORATORY ERROR"

To the Editor.—In the Feb. 7 issue of The Journal, page 653, the reviewer of the book "Electrolyte Changes in Surgery" compliments the authors on their statement "that the most common electrolyte abnormality encountered in clinical medicine is the 'laboratory error.' " Excellent methods are now available for maintaining quality control in clinical laboratories.

As a clinical pathologist, I have reviewed more than 2,000 complete electrolyte studies (determination of pH; carbon dioxide content; concentration of sodium, potassium, chlorides, and total proteins; and the hematocrit reading) during the past two and one-half years. This review showed that the most common electrolyte abnormality encountered in our clinical practice was that due to patient disease. The second most common electrolyte abnormality was that due to therapeutic excess or neglect.

With proper use of control serum samples, the probability of "laboratory error" in any electrolyte determination can be statistically quantitated and kept below a predetermined level. The probability of error within a certain range of values can readily be kept below 1 in 1,000. This easily attainable probable incidence of error is certainly far removed from a level that would make "laboratory error" the most common cause of electrolyte disturbances.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Privileged Communications: Admissibility of Hospital Record Made by Attending Physician.—This was an action for damages suffered by the plaintiff as a result of an automobile accident. From a judgment for the plaintiff, the defendant appealed to the Supreme Court of Iowa.

Among other things the defendant contended that the trial court erred in refusing to admit in evidence the medical record of the plaintiff made at the hospital where he was taken immediately after the accident. The record was made in the handwriting of the attending physician, who also testified that he examined and prescribed for the plaintiff. The record was denied admittance in evidence on the ground that it constituted a privileged communication.

The Iowa law relative to privileged communications provides that: "No practicing attorney, counselor, physician, surgeon, or the stenographer or confidential clerk of any such person, who obtains such information by reason of his employment . . . shall be allowed, in giving testimony, to disclose any confidential communication properly entrusted to him in his professional capacity, . . ." The plaintiff contended that the record clerk of the hospital is the stenographer or confidential clerk of the attending physician and that the records in her charge taken in a professional capacity, or information gained while acting in such a capacity, are privileged.

We think there is much merit in this contention, said the Supreme Court. We have previously announced the rule that we will draw no fine lines as to whether a communication, professionally secured, is necessary or unnecessary. The policy of the statute is to provide for great freedom of disclosure by a patient to his physician, for the patient is often in no position to know what disclosures may or may not be necessary for his proper treatment. We have also held that the statute should receive a liberal construction designed to carry out its manifest purpose to make consultation by a patient with his physician entirely confidential and free from anticipation or fear that this confidence will be broken by the examination of the physician, directly or indirectly, as a witness in some legal proceeding. Clearly, then, such a statute is intended to cover any information gathered from the patient and placed in a record by an attending, consulting, or treating physician, whether done intentionally, willfully, or under a law requiring its preservation. It is our conclusion that any such information placed upon such hospital records would be, and is, covered under the statute as privileged to the same extent that the knowledge and information of the examining or treating physician is privileged.

The defendant also contended that the attending physician should have been permitted to answer questions as to whether or not the plaintiff, when seen in the hospital, was a drug addict; whether or not the plaintiff gave a history of drug addiction; and whether or not examination of the plaintiff indicated him to be a drug addict. Answers to these questions were not permitted on the ground that they were privileged, but the defendant contended that the observations inquired of and made by the doctor were of the nature of a casual observation and that he could make that determination without the confidence or any confidential relationship with the plaintiff.

There can be no serious contention, said the Supreme Court, that a professional physician-patient relationship was not established or intended to be established when the information and observation which was solicited by these questions was secured by the doctor. It may well be that this doctor or any doctor could identify a person addicted to the drug habit if he saw him on the street, but such is not the case before us. The information imparted, or which could have been imparted, certainly had, or could have had, a definite relation to his treatment, or possible treatment, and was not in the class of information willingly imparted as to matters foreign to the professional service anticipated, such as how or where the accident happened. The information sought was obtained during the professional relationship between the doctor and the plaintiff and was privileged.

The defendant's other contentions were also overruled and the judgment in favor of the plaintiff was affirmed. *Newman v. Blom,* 89 N. W. (2) 349 (Iowa, 1958).

Hospitals: Liability for Self-Inflicted Injury to Mentally Disturbed Patient.—This was an action for damages to a patient resulting from the alleged negligence of the employees of the defendant hospital. From a judgment in favor of the hospital the plaintiff appealed to the Supreme Court of Minnesota.

The plaintiff was hospitalized in the defendant hospital for the purpose of receiving care and treatment for injuries resulting from an automobile accident which occurred a few days prior to admission. No mention was then made of any mental disturbance or distress afflicting her. She was apprehensive and depressed for a few days, but about four days later she had progressed sufficiently to be able to go home. On the day she was to leave she was visited by a relative and a minister, and she seemed to enjoy talking to both of them. Shortly after the second visitor had left the plaintiff jumped out of the hospital window and sustained the injuries forming the basis for this suit.

At the trial the plaintiff called a specialist in psychiatry and neurology. His testimony, based on the hospital record that was read to him, was to the effect that it would be impossible for any nurse to recognize suicidal tendencies on the part of the plaintiff and that even as a psychiatrist he might not have noticed such tendencies. Another doctor called by the plaintiff stated that he had observed the plaintiff while she was in the hospital and had not noticed any unusual behavior on her part.

The defendant is a general hospital and has no ward or department nor any special equipment for the care of psychiatric or mental patients and does not accept such patients. On its staff it has several neurosurgeons and psychiatrists. It is the place where its staff doctors bring their patients for care, and the doctors, not the hospital, direct the care to be given such patients. The psychiatrists on its staff come in as consultants to other doctors but do not hospitalize their psychiatric patients there. If a patient manifested a mental disorder, the patient's doctor would immediately be advised to such effect, and the hospital would arrange for the transfer of such a patient to some mental hospital. The defendant is not equipped with portable window bars or cages for the restraint of mental patients. There are no locks on the windows. If a patient manifests suicidal tendencies, a report to such effect would be made to the patient's doctor, and the hospital employees would carry out his instructions in the case. Under no circumstances would they attempt to restrain, tie up, or imprison any patient without an order to do so from the patient's doctor, except in extreme emergencies.

In this case, said the Supreme Court, there was nothing to indicate that the plaintiff was contemplating suicide. On March 31, while still apprehensive, she appeared able to control herself rationally and was cheerful about the prospect of returning home that day. She enjoyed talking to the minister who visited her that day and was reluctant to have him leave. She also manifested pleasure at the visit of her relative. To hold, the court continued, that under such circumstances the failure of the hospital attendants to apply restraints or to take other steps to restrict or confine her on their own responsibility constituted negligence would place too heavy and dangerous a burden on attendants employed by a general hospital. The Supreme Court concluded that in a case where a patient is admitted to a general hospital merely for the treatment of injuries sustained in an accident and nothing is said about any mental disorders afflicting such patients, and where, after such an incident as described here, the patient manifests such improvement as to eliminate any evidence of peculiarity or tendency to suicide and the hospital attendants abide by the orders of the patient's physician, it can scarcely be said that a fact in issue is present as to the hospital's negligence.

Accordingly the judgment in favor of the defendant hospital was affirmed. *Clements v. Swedish Hospital,* 89 N. W. (2) 162 (Minn., 1958).

Autopsies: Right of Non-M.D. to Give Opinion as to Cause of Death.—This was a prosecution for first-degree manslaughter. From a judgment of conviction, the defendant appealed to the court of appeals of Alabama.

The evidence showed that the autopsy on the body of the deceased had been performed by Mr. Sowell, a staff member of the State Department of Toxicology and Criminal Investigations. He held a bachelor of science degree in chemistry and additionally had studied bacteriology and human anatomy, pathology, physiology, and toxicology. He testified that he had performed approximately 500 autopsies during the time he had been employed by the department. He was not a physician, and the defendant contended that it was error to permit him to give his opinion testimony as to the cause of the deceased's death.

In view of Mr. Sowell's studies and experience, said the court, we think he was shown to be amply qualified to testify as an expert in this field.

For this and other reasons, the judgment of conviction was affirmed. *McMurtrey v. State,* 101 S. (2) 88 (Ala., 1957).

Charitable Hospitals: Immunity from Tort Liability.—This was an action for damages caused by the alleged negligence of the defendant hospital. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Pennsylvania.

While she was a patient in the defendant hospital, the plaintiff's wife fell and fractured an ankle. The defendant raised as its defense that it was an eleemosynary institution and thus not liable for the torts of its agents and employees.

The immunity of an eleemosynary institution from tort liability, said the Supreme Court, has long been the established rule in Pennsylvania. The rationale of the rule lay in the bounden duty of a public charity as a trustee to apply its funds in furtherance of its beneficent purpose. The doctrine has been abandoned in England and in a number of American jurisdictions but the law on this subject is clear in this state. Charitable institutions are not subject to liability for tort.

Even though the rule of nonliability is judge-made it should not be abrogated otherwise than by a statute made to operate prospectively.

The court therefore refused to repudiate the rule of nonliability, and the judgment in favor of the defendant hospital was affirmed. *Knecht v. Saint Mary's Hospital,* 140 A (2) 30 (Pa., 1958).

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Effects of Sublingual Nitroglycerin on Pulmonary Arterial Pressure in Patients with Left Ventricular Failure. J. B. Johnson, A. Fairley and C. Carter. Ann. Int. Med. 50:34-42 (Jan.) 1959 [Lancaster, Pa.].

The authors studied with the aid of right heart catheterization the hemodynamic alterations produced by glyceryl trinitrate (nitroglycerin) administration in 9 men and 4 women, between the ages of 35 and 74 years, with left ventricular failure. Most of the patients had hypertensive heart disease. After control cardiac outputs and blood pressure measurements in the brachial and pulmonary arteries were made, glyceryl trinitrate in doses of 0.6 mg. was administered sublingually. Cardiac outputs and blood pressure measurements then were repeated at short intervals during the succeeding 30 minutes. In 9 of the 13 patients a reduction in pulmonary artery pressure was noted within 5 to 15 minutes after the administration of glyceryl trinitrate. By the end of 30 minutes a reduction in pulmonary artery pressure was observed in all 13 patients. In 4 patients in whom it was possible to measure the pulmonary wedge pressure according to Hellem's method, a significant fall in this pressure was also observed. In 12 patients the total pulmonary resistance fell promptly during the first 15 minutes after glyceryl trinitrate therapy. There was no consistent alterations in the cardiac output, nor was there a significant increase in heart rate.

One patient with a clinical diagnosis of angina pectoris was catheterized as a part of a preoperative study in preparation for pericardial poudrage. A typical attack of anginal pain with radiation into the left arm, similar to the patient's well-documented previous attacks, occurred during the period of control hemodynamic observations which preceded the sublingual administration of glyceryl trinitrate. During the height of precordial pain there was a sharp increase in the pulmonary artery pressure, and the pulmonary resistance was greatly elevated. Administration of glyceryl trinitrate resulted in a prompt reduction of pulmonary artery pressure and total pulmonary resistance, and there was complete disappearance of anginal pain. The patient had no subsequent complications as a result of this experience. The clinical and physiological data obtained in this and other patients in this series after the administration of glyceryl trinitrate suggest that this drug has an important place in the management of patients with pulmonary artery hypertension and paroxysmal dyspnea associated with failure of the left ventricle.

Miliary and Meningeal Tuberculosis: A Review of 354 Cases. L. V. Reilly. Ulster M. J. 27:146-157 (Nov.) 1958 [Belfast, Northern Ireland].

Three hundred fifty-four patients were treated in the Whiteabbey Hospital, of the Northern Ireland Tuberculosis Authority, from late in 1947, when streptomycin first became available, to the end of 1956. The group included 76 patients with miliary disease alone, 160 with meningeal disease in whom miliary spread was not detected, and 118 with miliary and meningeal disease combined. The incidence of miliary and meningeal tuberculosis was highest in children under 4 years of age; these numbered 120. Sixty per cent of the adults were between 20 and 30 years of age. Five patients were over 60. A history of contact with a patient who had infectious tuberculosis was obtained in many patients, particularly in children.

The diagnosis of miliary tuberculosis was usually confirmed by roentgenologic evidence and by the detection of choroidal tubercles. These tubercles were found in 25 patients with only miliary disease, in 59 with combined miliary and meningeal disease, and in 8 with meningeal disease. Sometimes they were not found till some weeks after the diagnosis had been made. The Mantoux reaction was almost invariably positive. Bacteriological confirmation of miliary disease was usually obtained by the finding of Mycobacterium tuberculosis in the fasting gastric residue. Positive cultures were found in 49 of the 76 patients with miliary tuberculosis. A few attempts were made to isolate the organism from blood or bone marrow, but without success. Confirmation of meningeal disease was obtained by examination of the cerebrospinal fluid. The combination of increase in the protein content and in cell count with reduction in the sugar content of the cerebrospinal fluid was the usual finding. Cell counts varied widely from 60 to 300, and lympho-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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cytes usually predominated. Examination of the cerebrospinal fluid for tubercle bacilli was carried out in all cases, and tubercle bacilli were isolated in 144 of 160 meningeal cases, in 110 of 118 combined miliary and meningeal cases, and in none of the miliary cases. In addition to direct smear examinations, cultures were made.

Methods of treatment changed. At first the routine treatment consisted of the intramuscular injection of streptomycin, and intrathecal administration was added when meningitis was present. During 1949 aminosalicylic acid was added to the treatment routine, and isoniazid came into use toward the end of 1952. Improvement in recovery rate, reduction in length of illness, and a lower incidence of complications became evident after the introduction of isoniazid. The addition of isoniazid to the treatment made it possible to dispense with the intrathecal use of streptomycin in many patients. A group of 37 patients treated with the 3 substances without intrathecal therapy made a full recovery. The most serious complication of meningitis was severe mental retardation, usually with blindness and deafness. Eleven of 178 patients with meningitis had this complication, and some of them still survive. Early diagnosis offers the best hope of recovery. A marked reduction in incidence of the disease occurred in the last few years.

Sickle Cell-Hemoglobin D Disease. E. W. Smith and C. L. Conley. Ann. Int. Med. **50**:94-105 (Jan.) 1959 [Lancaster, Pa.].

The authors report a youth with sickle-cell–hemoglobin D (S-D) disease, who was followed up from the age of 14 months to that of 21 years. The patient had fair skin, blue eyes, blond hair, and sthenic habitus, and he had no features suggestive of Negroid ancestry. He had had recurrent episodes of severe pain in the back and extremities dating from early infancy, and many attacks of "pneumonia," transient ulcers of the lower legs, and a chronic hemolytic anemia. Nevertheless, he maintained the general appearance of good health and was an accomplished athlete. Examination of a fixed blood smear revealed pronounced anisocytosis, with a large number of target cells and a few sickle cells, and the electrophoretic pattern of the hemoglobin on filter paper at pH 8.6 could not be distinguished from that of sickle-cell anemia. Despite these findings a diagnosis of homozygous sickle-cell disease was questioned because of many atypical features. Additional studies were performed, which revealed clear separation of the S and D hemoglobin components on agar plates at pH 6.2, and a smaller component with the mobility of fatal hemoglobin was also observed. The mother of the patient and 5 of her relatives were found to have the hemoglobin D trait. The patient's father and 6 of his relatives had the sickle-cell trait. In neither lineage was there evidence of Negro ancestry. Since the patient's paternal grandfather married twice and S hemoglobin appeared in children of each marriage, it is almost certain that he carried the S gene. The atypical hemolytic disorder in the patient thus had resulted from the inheritance of hemoglobin D from the mother and hemoglobin S from the father. The genetic data which were obtained support the belief that hemoglobin D is an allele of types A, C, and S of hemoglobin.

Salt Metabolism in Hypertension. J. M. Weller and S. W. Hoobler. Ann. Int. Med. **50**:106-114 (Jan.) 1959 [Lancaster, Pa.].

It is an established fact that sodium chloride metabolism is abnormal in patients with essential hypertension. These patients may have a slightly elevated serum sodium concentration, expanded total body sodium content, and increased amounts of sodium and water in their arterial walls. Hypertension may be alleviated by sodium depletion. The authors' studies carried out at the University Hospital in Ann Arbor, Mich., confirmed the fact that chlorothiazide, a potent natruretic agent, may exert an antihypertensive effect in both hypertensive animals and in patients. This drug potentiates the effect of various antihypertensive regimens. The concomitant administration of chlorothiazide reduces the requirement for ganglionic blocking agents in the treatment of hypertension. Patients who have undergone sympathectomy appear to be unusually responsive to the lowering effect of chlorothiazide on the blood pressure.

The increased renal tubular rejection of sodium, chloride, and water in response to salt loading, which is present in patients with essential hypertension, is felt to be the result of the elevated blood pressure and not its cause. There is no evidence that water excretion, occurring in excess of sodium excretion, causes a "relative retention" of sodium in most of the patients with hypertension. The concept is discussed that in essential hypertension the sodium content of certain compartments or tissues, possibly including vascular smooth muscle, may be increased. This may lead to the rise in blood pressure. The effectiveness of chlorothiazide in the treatment of some patients with hypertension may be through its ability to deplete these tissues of sodium; in other patients it appears to act through depletion of the plasma volume.

Cholesterol Metabolism: Clinical Aspects. H. Malmros. Nord. med. **61**:3-7 (Jan. 1) 1959 (In Swedish) [Stockholm].

In essential hypercholesterolemia (Müller's disease) the hereditary disturbance in cholesterol metabolism can lead to considerable deposits of cholesterol in various tissues. Particularly in the cases in which the serum cholesterol content is around

400 mg. % or more, Müller's disease may be suspected as the cause. Examination of the serum cholesterol in siblings and other relatives may reveal several cases of cholesterolemia in the family. Such investigations are of practical value from the prophylactic standpoint, as in patients with hypercholesterolemia on a hereditary basis there is special risk of heart infarction or other grave manifestations of arteriosclerosis setting in early. Hypercholesterolemia can appear secondarily in other diseases, such as hyperthyreosis, nephrosis, and poorly regulated diabetes. Here cholesterol deposits may occur in different tissues. This is also true in cholesterolemia seen in essential or secondary hyperlipemia. Cholesterol deposits can occur without increased serum cholesterol, as in Hand-Schüller-Christian disease. Most gallstones are made up chiefly of cholesterol. Not infrequently there is xanthelasma palpebrarum in women with gallstones. The level of serum cholesterol in these cases is often increased. From the clinical point of view the most important cholesterol deposits are those which appear as atheromatous plaques in the intima of the arteries in arteriosclerosis. During the last 2 or 3 years in the department of medicine at Lund, 30 patients with essential hypercholesterolemia were treated, most of them for over a year, with a diet containing no fat except corn oil. A definite fall in serum cholesterol was noted after a few weeks.

Sideropenia Problem Illuminated by Follow-Up of Patients with Hypochromic Anemia. I. Lindblom. Nord. med. 61:7-13 (Jan. 1) 1959 (In Swedish) [Stockholm].

Of 305 patients with sideropenia (25 men and 280 women) treated 20 years ago, 80 have died; one death was due to cancer of the esophagus. Of the 123 patients followed up, 117 of whom were women, 2 had developed cancer of the hypopharynx (at present healed), and 1 had developed sublingual cancer (operated on 5 years ago and cured). Because of membranes of the hypopharynx which seem to be relatively resistant to therapy, 20 patients have been regarded as especially predisposed to cancer; they have required after-control, possibly combined with biopsies of specimens from the mesopharynx and the nasopharynx, in order, if possible, that precancerous conditions may be revealed early. The frequency of other symptoms of sideropenia is higher here than in other patients, but the symptoms have responded in the same degree to treatment with iron. While no relation between sideropenia and dietary deficiency has been established, the possibility of deficient diet to some extent years ago and in occasional cases now is not excluded. Graver recurrence of sideropenic anemia depends on acute causes, particularly bleeding. Return to normochromia occurs only gradually with increasing age, probably as a sign of slow building up of the iron depot. The irreversibility of sideropenia symptoms is greater in the patients initially treated only for their anemia and in those discovered through family connections than in the patients accidentally discovered to have the disease. A similar clinical course in the 3 pairs of uniovular twins in the material further supports the hypothesis that a dominant gene transmits the tendency to insufficient absorption of iron, disclosed especially when large amounts of iron are lost through bleeding.

Pernicious anemia was found in 10.6% of all the patients followed up in the series, and in 26% of those with stationary achlorhydria. Clinical observations on the 117 women suggest that hereditary factors, marginal amounts of iron in the diet, and pathological bleeding are conditions to be considered. Particularly in adolescent girls these conditions seem likely to cause sideropenia, which will recur on slight extra demands on the iron deposits.

Familial Hypercholesterolemic Xanthomatosis and Hypothyreosis. J. Opstad. Nord. med. 61:15-17 (Jan. 1) 1959 (In Norwegian) [Stockholm].

A case of familial hypercholesterolemic xanthomatosis and myxedema in a man, aged 42 years, belonging to a family with familial hypercholesterolemia, was observed for a year. The serum cholesterol concentration varied during treatment with thyroxin. After a transient fall 3 months after the thyroid function had become normal, the concentration rose to values considerably higher than those before treatment. The phenomenon is believed to depend on the patient's abnormal cholesterol metabolism. The author had previously reported a case of familial hypercholesterolemic xanthomatosis combined with myxedema in which there was an initial fall in the serum cholesterol concentration after treatment; 3½ years later, however, the serum cholesterol level was 390 mg. %, although the patient was euthyroid and metabolism was normal. It appears that thyroxin treatment of patients with familial hypercholesterolemic xanthomatosis and myxedema does not result in long-range reduction of the serum cholesterol, but a fall in the serum concentration occurs early or late during treatment and is followed by a secondary increase of serum cholesterol.

Hypoglycemic Effects of 1-(p-Chlorobenzenesulfonyl)-3-n-Propylurea: Observations in Man. A. M. Tornow, M. R. Zinke, P. Greenberg and C. M. Leevy. Diabetes 8:1-6 (Jan.-Feb.) 1959 [New York].

The authors report on 33 patients with diabetes mellitus who were treated with *chlorpropamide* [1-(*p*-chlorobenzenesulfonyl)-3-n-propylurea] for periods varying from 6 weeks to 6 months. Of the 33 patients, 18, who were controlled on diet and tolbutamide, or less than 20 units of insulin, were considered to have mild diabetes; 7, requiring 20 to 60 units of insulin, were considered to have moderate diabetes; 5 with maintained hyperglycemia and glycosuria on 60 or more units of insulin were considered to have severe diabetes; and 3 with unpredictable fluctuation between hyperglycemia-glycosuria-ketonuria and insulin shock were considered to have brittle diabetes. Two of the 18 patients with mild diabetes, who were previously controlled on tolbutamide, were no longer responsive to this drug at the time chlorpropamide therapy was instituted. During the earlier part of the investigation, each of the patients was given 1 Gm. of chlorpropamide daily; subsequently the daily dose varied between 0.25 and 0.5 Gm. depending on its effectiveness.

Results showed that chlorpropamide is an effective hypoglycemic agent in patients with diabetes mellitus. Chlorpropamide exhibited only a slightly greater hypoglycemic effect than tolbutamide after single doses of 1 Gm. of these drugs, but it appeared to be significantly more potent when given in maintenance doses of 0.5 to 1 Gm. daily. It permitted stabilization of diabetes in 2 patients who had become refractory to tolbutamide and in 4 patients with incomplete control on tolbutamide. There is, in general, an inverse relationship between the level of chlorpropamide and its effects on the concentration of sugar in the peripheral and hepatic venous blood. The drug tends to accumulate, so that adjustment of dosage is necessary to prevent profound drop in blood sugar. Severe hypoglycemia occurred in 3 patients on maintenance doses of 1 Gm. daily, associated with mental confusion, tachycardia, and sweating. Reduction of the administered amount and of the frequency of administration of the drug prevented recurrent hypoglycemia.

Chlorpropamide did not produce any evidence of dermal, renal, hepatic, or hemopoietic toxicity in the 33 patients. A regimen consisting of an initial dose of 0.5 Gm. of chlorpropamide each day, followed by a reduction or an increase depending on the clinical response, provided quickest control and fewest side-reactions. Slight gastrointestinal reactions were observed in 6 patients receiving 1 to 2 Gm. of the drug each day. Best control was established by periodic determinations of blood sugar and sulfonamide levels.

The Use of Latex Agglutination Reaction in the Diagnosis of Rheumatoid Arthritis. A. Ulloa, S. W. Griffin, M. L. Hayes and H. L. Holley. J. M. A. Alabama 28:212-214 (Jan.) 1959 [Montgomery].

The serum of patients with rheumatoid arthritis is capable of agglutinating sensitized particulate bodies, such as bacteria, erythrocytes, collodion, and latex particles. This agglutination capacity is predicted upon the presence in the serum from rheumatoid patients of factors that are either absent or present in minimal amounts in the serum of normal individuals. Such a factor has been identified in the gamma globulin component of rheumatoid serums with the use of the analytic ultracentrifuge, paper chromatography, and ion exchange chromatography, in addition to the variety of serologic indicator systems. The exact nature of this so-called rheumatoid factor remains obscure, but the fact that it appears consistently in the serum of rheumatoid patients and rarely in that of nonrheumatoid patients represents one of the most significant advances. Since Rose and coworkers in 1948 used sensitized sheep cells in the first serologic test for rheumatoid arthritis, many modifications have been suggested.

The authors report their experiences at University Hospital and Hillman Clinic in Birmingham, Ala., with the latex test in which whole serum is used. Tests were made on 171 persons, in 85 of whom the diagnosis of rheumatoid arthritis was definite, and in 9 probable. Twenty-three had osteoarthritis; 9, lupus erythematosus; 10, ankylosing spondylitis; and 5, gouty arthritis. The other groups included normal controls and patients with disorders other than rheumatoid arthritis. The test was positive in 75 of the 85 patients (88%) with known rheumatoid arthritis. The authors conclude that the latex test is a valuable aid in the diagnosis of rheumatoid arthritis.

SURGERY

Massive Systemic-Pulmonary Arterial Shunt Through Multiple Pleural Adhesions. P. T. De Camp and H. B. Hatch Jr. A. M. A. Arch. Surg. 78:206-211 (Feb.) 1959 [Chicago].

The authors report on a 34-year-old woman in whom a massive systemic-pulmonary arterial shunt occurred through multiple arterialized pleuropulmonary adhesions between the wall of the chest and the upper lobe of the left lung. This shunt increased the resting cardiac output by 75% and produced repeated attacks of choking and syncope. Preoperative roentgenograms of the chest revealed old fibrotic lesions in both lungs in the region of the lateral portions of the first and second anterior interspaces. A phonocardiogram recorded over the left third interspace near the sternal border showed a long systolic bruit with midsystolic accentuation. Division of the pleuropulmonary adhesions resulted in relief of all symptoms and eradicated the abnormal shunt.

Vascularized pleuropulmonary adhesions are commonly found at thoracotomy, and in some patients a pulsatile flow occurs from divided vessels. Vigorous pulsatile flow must indicate a systemic arterial communication, and the direction of the blood flow must be from the thoracic wall into the lung. The findings in this patient indicate that a considerable quantity of such blood may flow back into the pulmonary artery. A systolic, or continuous, murmur or souffle is characteristic, as is the roentgenographic evidence of notched adjacent ribs if intercostal arteries have sufficiently enlarged. The shunt may significantly increase the myocardial work load. If enough blood is deviated from the normal systemic pathways, syncope and other symptoms of cerebrovascular insufficiency may develop. Right heart catheterization may detect such a shunt, and is recommended in patients in whom this condition is suspected. In selected cases aortography may give additional information.

Surgical Treatment of Chronic Bilateral Disease of the Lungs. S. L. Libov and Z. I. Levina. Khirurgiya 35:13-19 (no. 1) 1959 (In Russian) [Moscow].

The possibilities of surgical treatment of certain bilateral diseases of the lungs are discussed. According to the literature and the authors' personal observations, bilateral disease of the lungs runs a severe course. In the series presented, 33 patients were examined; 27 of these patients suffered from bronchiectasis, and 26 were operated on. Bilateral operations were performed on 14 patients (single-stage operations were carried out in 3 instances). The greatest number of removed segments was 12. The left lung and the medial lobe of the right were removed in one patient. The majority of the two-stage operations were carried out at an interval of 6 months. Three patients died, one after a single-stage operation. All operations were performed with the patients under intratracheal oxygen-ether anesthesia.

Surgical Considerations of Peripheral Arterial Aneurysms: Analysis of One Hundred Seven Cases. E. S. Crawford, M. E. DeBakey and D. A. Cooley. A. M. A. Arch. Surg. 78:226-238 (Feb.) 1959 [Chicago].

The authors report on 107 patients with peripheral arterial aneurysms, who were operated on in the surgical services of the Jefferson Davis, Veterans Administration, and Methodist hospitals in Houston, Texas, during the past 5 years. Of the 107 patients, the peripheral arterial aneurysms were caused by arteriosclerosis in 54 and by trauma in 37; poststenotic aneurysms of the subclavian artery, just distal to a constriction produced by the anterior scalenus muscles, occurred in 3 patients; aneurysms occurred in 7 peripheral homografts, employed in the treatment of patients with occlusive lesions of the femoral artery, 8 to 26 minutes after the operation; the causative factor in the development of false aneurysms occurring after peripheral arterial operations in 6 patients was a combination of infection, tension at the suture line, and fraying associated with the use of the Edwards-Tapp nylon tube. Of the 54 arteriosclerotic aneurysms, 30 were located in the popliteal artery, 23 in the femoral artery, and 1 at the bifurcation of the innominate artery. The relatively high incidence of multiple lesions in this group of peripheral arteriosclerotic aneurysms is evident from the fact that more than one aneurysm was present in 26 of the 54 patients. Of the 37 patients with traumatic aneurysms, the aneurysm resulted from a gunshot wound in 25 and from a stab wound in 12. The traumatic lesions were widely distributed, but in 29 patients (80%) the aneurysm involved an artery necessary for normal blood flow, such as the carotid, brachial, femoral, popliteal, or subclavian.

The clinical manifestations of the disease varied according to the type of lesion. The age of the patients with arteriosclerotic aneurysm ranged from 45 to 85 years; these patients were considerably older than the others and frequently had associated heart disease and hypertension. The presenting symptom in most of the patients, regardless of the type of lesion, was a pulsating mass. Thrombosis was present in a significant number of patients, and this complication was associated with arterial insufficiency in all patients. Rupture had occurred in 8 patients with arteriosclerotic aneurysms, and heart failure was present in 3 patients with arteriovenous fistulas. The lesion was localized to an operable segment of artery in all patients, and treatment was directed at both excision of the lesion and restoration of circulation. The aneurysms were excised in all patients, and restoration of circulation was possible by end-to-end suture of the involved segments in 45; 14 of the latter patients had arteriosclerotic, 29 had traumatic, and 2 had poststenotic aneurysms of the subclavian artery. The defect remaining after excision of the lesion in the other patients was of sufficient length to require an arterial substitute to restore peripheral circulation. Homografts, Dacron tubes, and the Edwards-Tapp tube were used for this purpose.

The results obtained in these patients were extremely gratifying, particularly when compared with the natural course of the disease. Normal circulation was restored in most of these patients. Amputation was required in only 6 patients, although a large number had arterial insufficiency and gangrene at the time of the operation. Death occurred in only 3 patients in this series, all of whom had arteriosclerotic aneurysms, despite the high incidence of associated heart disease and hypertension. Of the 3 patients who died, death resulted from myocardial infarction in 2 who were operated on for rupture of the aneurysm, and death resulted from air embolism in the third patient. Although the follow-up period has been over 3½ years in most patients, the results have been well maintained. Three patients with arteriosclerotic aneurysm have died since operation, 1 of a ruptured aortic aneurysm, 1 of myocardial infarction, and 1 of cancer. Arterial occlusion has occurred in only 3 patients, and amputation has not been required by any of the patients since discharge from the hospital.

Arteriovenous Aneurysm of the Lung. D. K. Ossipov. Khirurgiya 35:8-13 (no. 1) 1959 (In Russian) [Moscow].

The author emphasizes that up to 1942 only a few reports were to be found in the literature regarding arteriovenous aneurysms of the lung revealed at autopsy. The signs and symptoms of these aneurysms are cyanosis, changes in the terminal phalanges of the fingers, and increase in the number of erythrocytes in the blood and of the hemoglobin percentage. These signs and symptoms may be very mild or may be entirely absent. The roentgenologic method of examination with tomograms, roentgenokymograms, and especially angiopneumograms is decisive in the diagnosis. Surgery is the only rational method of treatment. The most sparing resection of the lung is recommended. The author presents the case histories of 2 women on whom lobectomy was performed in connection with arteriovenous aneurysms of the lung. One patient was operated on under local anesthesia, and the other under intratrachael oxygen–ether anesthesia.

Idiopathic Mediastinal Fibrosis. N. R. Barrett. Brit. J. Surg. 46:207-218 (Nov.) 1958 [Bristol, England].

The author points out that, while some observers accept mediastinal fibrosis as the expected end-result of tuberculous mediastinal adenitis, syphilis, radiotherapy, or some comparable process, he argues that there is an idiopathic form which differs from fibrosis known to have been caused by chronic granulomatous conditions. He uses the term "idiopathic mediastinal fibrosis" because the etiology is unknown, because the site of the changes is the mediastinum above the heart, and because an abnormal proliferation of fibrous tissue is the visible anomaly. The clinical hallmark is the presence of venous hypertension in the catchment area of the superior vena cava. This hypertension is due to a fibrous mass that engulfs, invades, and destroys some or all of the great veins uniting to form the superior vena cava. The disease is rare, but it afflicts people of all ages and of both sexes; in general, the onset occurs in middle or late life.

As a rule, the symptoms of idiopathic mediastinal fibrosis appear suddenly in a patient who has previously been healthy. At the beginning, superior caval obstruction is neither suggested nor obvious in many cases. The first symptoms are often intermittent and, being relatively mild, may pass unheeded. In a typical case, the first symptom is puffiness of the face and arms, noticed especially when the patient gets up in the morning. In the second clinical phase, when the effects of superior caval obstruction are at their height, the following signs are added: a dusky color of the face, neck, and arms, with suffusion of the conjunctiva and perhaps telangiectasis; dyspnea, giddiness, tinnitus, headache, epistaxis, or hemoptysis; a feeling of pressure in the head; and a dislike of crowded places. All these unpleasant features are aggravated by coughing, straining, stooping, or exercise. After about 6 to 9 months the patient enters upon the third phase in which, as the years pass, there is a progressive relief of many signs and symptoms, but he never again becomes totally free from disability. The patient usually remains ambulant.

It is suggested that the pathological changes of idiopathic mediastinal fibrosis are akin to those found in periureteric fibrosis, pseudotomor of the orbit, and possibly ligneous thyroiditis (Riedel's disease). Idiopathic mediastinal fibrosis is a self-limiting disease, in which the signs and symptoms of superior caval obstruction are replaced and mitigated by those associated with the growth of a collateral venous circulation. The disease seldom kills; it is compatible with a long life, although the individual's working capacity may be somewhat restricted. There is no medical treatment. Irradiation is of no avail, and surgical operations have proved to be almost uniformly unsuccessful. The failure of bypass and replacement grafts is due to thrombosis in the grafts, and at the moment it seems to be impossible to prevent this.

Defects of the Interventricular Septum in Infancy: A Two-Stage Approach to Their Surgical Correction. H. D. Sirak, D. M. Hosier and H. W. Clatworthy, Jr. New England J. Med. 260:147-151 (Jan. 22) 1959 [Boston].

The high mortality of open-heart surgery for defects of the interventricular septum in infants may be avoided by a two-stage approach. Surgical treatment is urgently needed in many of these small patients, weighing less than 4.5 kg. (10 lb.), because of heart failure or recurrent respiratory infections that do not respond satisfactorily to medical therapy. A two-stage approach is proposed to increase both the immediate and the ultimate salvage rate in these patients and still avoid the high mortality of open-heart surgery in infancy. In the first stage, which is performed in infancy, the pulmonary artery is narrowed by being encircled with a band of plastic cloth, similar to that in the method of Muller and Dammann. The constriction increases resistance to outflow from the right ventricle. This, in turn, reduces the left-to-right shunt across the septal defect. Thus, the work of the left ventricle is decreased, systemic circulation is improved, and the lung vasculature is spared. The second stage is the corrective open-heart repair. At this time the septal defect is closed, and the constriction is removed from the pulmonary artery. The operation is performed after the child has grown large enough to tolerate cardiac bypass.

A 3-month-old infant was hospitalized in July, 1955, because of recurrent heart failure and pneumonia. Fluoroscopy showed that the activity of the pulmonary arteries was markedly increased. The patient remained in the hospital where he had recurring bouts of heart failure and respiratory infection. When he finally improved, cardiac catheterization was undertaken. This showed a defect of the interventricular septum, with moderate pulmonary hypertension and a large left-to-right shunt. On Dec. 1 a pulmonary tuck was performed. After the patient returned home, growth and development progressed normally until 2 years of age, when the parents noted that he became somewhat bluish on exertion. During the next 6 months the cyanosis gradually became constant, and at 28 months of age he was readmitted. Open-heart surgery was performed on Jan. 15, 1958, and the child was discharged on the 12th postoperative day. Recatheterization 2 months later indicated a return to normal hemodynamics. The authors believe that this is the first patient in whom both stages of the two-stage approach to the surgical correction of defects of the interventricular septum were successfully completed. Success depends upon proper selection of patients and an adequate reduction of the pulmonary artery lumen during the first stage.

Bacterial Endocarditis After Surgery for Acquired Heart Disease: Report of Two Cases and Review of the Literature. F. G. Hoffman, S. L. Zimmerman, E. A. Bradley and B. Lapidus. New England J. Med. 260:152-158 (Jan. 22), 1959 [Boston].

The cases of 38 patients in whom bacterial endocarditis developed after cardiotomy for acquired heart disease were collected from the literature, and 2 new cases are described in detail. The ages of the patients ranged from 20 to 51 years. Mitral valve surgery, including commissurotomy and suturing, was performed on 23 patients, aortic valve surgery (which included commissurotomy and nylon ball) on 21, and combined aortic and mitral valve surgery on 4. Cardiotomy without commissurotomy was carried out on one patient. Inquiry into the type of prophylactic antibiotic treatment before hospitalization for cardiotomy revealed information for only 7 patients, but the authors feel that further investigation of this point might be helpful. Staphylococcus pyogenes var. aureus was the causative organism in 26 cases; 11 were coagulase-positive, and 15 were coagulase-negative. Of the 11 patients with coagulase-positive staphylococci, 6 are living, and 5 dead. Of the 15 patients with coagulase-negative organisms, 7 are living, and 8 dead. These figures suggest only that coagulase-negative strains predominate and carry a higher mortality.

An attempt was made to correlate the possible source of infection with the temporal relations of onset of bacterial endocarditis after cardiotomy. Evidence suggests an extracardiac source when bacterial endocarditis develops within the first 4 weeks after operation, whereas in patients in whom the disease develops later, it is usually difficult to demonstrate the source. Further studies on the healing process of the surgically traumatized valves appear indicated. The frequency of postcardiotomy bacterial endocarditis can only be estimated, but it appears to be well under 1%. In the series studied, treatment regimens varied greatly. Almost all patients received penicillin, but streptomycin, tetracyclines, and chloramphenicol were combined with about equal frequency, apparently depending on in vitro sensitivity. The absolute mortality rate seemed to be about 35%, the corrected mortality about 27%. Previous reports on staphylococcic endocarditis not related to heart surgery gave a mortality rate of about 50%. No definite correlation between valvular calcification and mortality could be determined.

The clinical picture of bacterial endocarditis after cardiotomy was atypical in this series and differed from the usual subacute bacterial endocarditis. Fever, often low-grade, and septicemia were the only consistent findings. Changing heart murmurs, pericarditis, splenomegaly, petechiae, and embolic phenomena occurred in only a few patients. The diagnosis proved difficult, but postcardiotomy endocarditis should be suspected in any patient with fever after cardiotomy in the absence of the usual signs of bacterial endocarditis.

NEUROLOGY & PSYCHIATRY

Five Year Report of the Cerebral Palsy Program at the Nebraska State Orthopedic Hospital. H. E. Mitchell and B. W. Drompp. Nebraska M. J. 44:3-10 (Jan.) 1959 [Lincoln].

The authors report on 275 patients who were accepted, examined, and treated as cerebral palsy patients between 1952 and 1957 at the cerebral palsy clinic sponsored by the State of Nebraska and located at the Nebraska Orthopedic Hospital in Lincoln. Of the 275 patients, 187 were between the ages of 1 and 3 years; the fact that between these ages it is obvious to the parents that the child is not following a normal pattern of development, due to the lack of ability to sit or walk properly, accounts for the greater incidence of referrals at this age. A far greater number should be referred at this time. There were only 14 patients, aged less than 1 year, and only 11 over 13 years of age. Two hundred three patients (74%) had the spastic type of cerebral palsy; 47 (16%), the athetoid type; 15 (6%), the mixed type; and 10 (4%) were ataxic. The disease was mild in 77 patients (38%), moderately severe in 137 (50%), and severe in 61 (22%). Quadriplegia was present in 167 patients (60%), right hemiplegia in 35 (13%), left hemiplegia in 30 (11%), paraplegia in 38 (14%), triplegia in 4 (1.7%), and monoplegia in 1 (0.3%). Thirty-four patients (12%) had an intelligence quotient of from zero to 50, 96 (33%) had an IQ of from 50 to 70, 132 (47%) had an IQ of from 70 to 100, and 24 (8%) had an IQ of over 100. The disease was suspected to be congenital in 54 (20%), caused by prematurity in 34 (12%), due to birth injury in 127 (46%), caused by meningitis and encephalitis in 33 (12%), and due to other causes in 27 (10%).

The treatment program consisted of a coordinated effort of physical training and rehabilitation, speech training, correction and improvement of hearing and visual disability, and educational opportunities. The physical training program consisted primarily of functional activities. In order to proceed from stage to stage of the training program, bracing may play a very important part. Although conservatism is the watchword in the treatment of cerebral palsy, the authors unhesitatingly recommend surgical treatment when it is indicated to combat contracture or to improve the function of an extremity. One hundred eighteen patients underwent one or more surgical procedures. Surgical treatment on the upper extremity was performed primarily to relieve pronation contractures of the forearm, and good results were obtained from simple pronator teres tenotomy. Surgical treatment to improve the function of the lower extremity was gratifying in many patients. Hamstring transfer according to Egger's technique combats knee flexion and also corrects much of the adduction and internal rotation deformity, if present; it is considered the method of choice for the relief of scissor gait. Of 40 patients subjected to such transfers, 38 obtained excellent or good results, and 2 fair results. Soleus neurectomy is prefered to gastrocnemius neurectomy for the treatment of persistent talipes equinus, and there will always be a number of cases in which lengthening of the achilles tendon will be the procedure of choice.

In this series operative stabilization of joints proved very useful. The end-results in 171 operations performed on both upper and lower extremities were satisfactory in all but 15 cases. Of 57 patients treated in the occupational therapy department specifically to improve hand function, only 4 showed exceptional improvement, 42 showed moderate improvement, and 11 showed little or no improvement. Of 58 patients treated by the speech therapist, 3 showed exceptional improvement, 26 showed moderate improvement, and 29 showed little or no improvement. The educational program of the patients was recently surveyed by a mail questionnaire. Of 116 patients who answered the questionnaire, 87 were of school age. Thirty-seven of the 87 patients were in a school grade comparable with age; the remainder were below grade level or were no longer in school. Three children graduated from high school, and 2 are now attending college.

GYNECOLOGY & OBSTETRICS

Carcinoma Cervix Uteri: An Increase in Five Year Survival Rate: From 20 to 55 Per Cent during Twenty Years. H. B. Hunt, L. S. McGoogan, R. A. Bunting and R. E. Waggener. Nebraska M. J. 44: 53-58 (Feb.) 1959 [Lincoln].

The authors studied the results of treatment in patients with carcinoma of the uterine cervix who were treated at the University of Nebraska Hospital in Omaha over a period of 20 years. Public education, earlier diagnosis, and more prompt and improved treatment contributed to the recent increase in the 5-year survival rate among patients with carcinoma of the uterine cervix. According to the Nebraska State Department of Health, the death rate from carcinoma of the uterine cervix declined from 11.5 per 100,000 population for the period 1944-1948 to 6.6 for the period 1954-1957. At the University of Nebraska Hospital the 5-year survival rate for all cases of carcinoma of the cervix increased from 20.5% in 1936 to 55.8% in 1952. The average time elapsing between the beginning of symptoms and first consulation during the period 1930-1937 was 11 or 12 months, as compared with 8 or 9 months for the period 1938-1947 and 7 or 8 months for the period 1948-1952. The interval between diagnosis and initiation of treatment has been reduced from 21 days during the period 1930-1937 to 10 days during the period 1948-1952.

All women past 40 should have a thorough pelvic examination annually. Cytological smears and biopsy are vitally important in the detection of carcinoma of the uterine cervix in its earliest stage. If cells of smears appear suggestive of or positive for cancer, a thorough evaluation of the entire cervical and uterine canal is indicated. Treatment should be individualized according to the patient's age and whether she wishes to bear children. In young women, extensixe conization of the cervix or trachelectomy, followed by frequent examinations with smears, is considered acceptable treatment. In older patients, total hysterectomy with removal of a rather wide cuff of vagina is recommended. If a major operation is contraindicated, roentgenologic treatment and radium irradiation would be the therapy of choice.

Of 111 patients with invasive carcinoma of the uterine cervix admitted to the University of Nebraska Hospital between 1948 and 1952, 102 were treated with radiotherapy alone, 5 with a combination of radiotherapy and surgery, and 4 with Wertheim's hysterectomy with radical lymph node dissection. Radiotherapy consisted of 2 or 3 applications of radium across the vaginal vault and along the uterine canal supplemented by external roentgenotherapy, delivered during a total period of 5 weeks. The survival rate among patients so treated was 54.7%. This is a great improvement over the survival rate of 20.5% for patients given intracavitary radium treatment alone during the period 1931-1936. The survival rate doubled to 41% during the period 1937-1947 when patients were referred earlier and received additionally external roentgenologic treatment. Improvement of radiotherapy was effected not through any increase in total dosage of radium or roentgen rays but through more individualization according to the distribution of disease, anatomy of the patient, and the general health and tolerance of the patient for irradiation.

There has been a recent revival of the surgical approach, and in the hands of the highly trained and technically skilled gynecologic surgeon the patient salvage for stage 1 carcinoma of the cervix is equal to that of the salvage with irradiation therapy. In stage 2 carcinoma of the cervix the survival rates after surgery are lower than those in stage 1; they are similar to those for irradiation therapy, but they are not greater. No proof has been presented that the superb operation of even the master surgeon excels or, in fact, equals contemporary radiotherapy of comparable excellence in the control of stage 1 and stage 2 cancer of the uterine cervix.

PEDIATRICS

Intestinal Polyposis with Oral Pigmentation (Peutz-Jeghers Syndrome): Report of a Case with Review. L. W. Falkinburg and M. N. Key. J. Pediat. 54:162-169 (Feb.) 1959 [St. Louis].

The authors report on a 5-year-old boy with intestinal polyposis and with abnormal pigmentation in and around the mouth. On admission to the Roger Williams General Hospital in Providence, R. I., the child complained of severe abdominal pain, nausea, and vomiting. Laparotomy was performed, and a large amount of clear serous fluid was found in the peritoneal cavity. In the mid-jejunum there was a large intussusception which was irreducible, and a mass interpreted as a polyp could be palpated inside. This segment of small intestine was resected, and an end-to-end anastomosis was performed. Examination of the operative specimen revealed a polypoid adenoma of the jejunum. The patient's recovery was uneventful, but 6 months later he was admitted to the hospital for a second time, complaining of abdominal pain, tarry stools, and repeated attacks of respiratory infections. On physical examination the boy was pale, and his lips were cyanotic. Numerous small blackish-purple, discrete spots were noted on the mucosal surface of the lower lip, on the mucosal surface of the cheek, and on the hard palate. Roentgenologic examination of the gastrointestinal tract showed evidence of jejunal polyposis. Three blood transfusions were given, and iron therapy was started. There was general improvement, and the patient was discharged 3 weeks later with a diagnosis of Peutz-Jeghers syndrome. The patient was readmitted to the hospital after 3 months because of severe abdominal pain, anorexia, nausea, and vomiting. Laparotomy was performed, and 2 jejunal polypoid adenomas were removed. Recovery was uneventful, and the patient was referred to the outpatient department for periodic observation.

Peutz-Jeghers syndrome is a combination of oral melanosis and small intestinal polyposis, in which frequently a definite hereditary factor can be demonstrated. In this patient the pigmentation was noticed and correctly interpreted only on the second hospital admission, after the patient had undergone, during a previous admission, a major operation for intestinal obstruction. Such pigmentation should be looked for in every case of small intestinal polyposis, and, conversely, the discovery of such areas of pigmentation in the course of physical examination should direct the attention of the physician to the gastrointestinal tract. The occurrence of polyps in the small intestine is sufficiently uncommon to arouse suspicion of the syndrome. The first concern in the treatment is usually the relief, by surgical removal, of the intussusception responsible for the acute intestinal attack. After the diagnosis has been established, the question arises as to whether polyps shown by roentgenograms should be removed electively. In considering elective polypectomy no general rule can be laid down, but each case must be carefully and individually evaluated. The anemia, which is the result of slow bleeding from the polyps, can be successfully treated by blood transfusions and the administration of appropriate iron compounds. No treatment has been suggested for the melanotic areas, which are asymptomatic in themselves and are not cosmetic problems.

BOOK REVIEWS

Psychotherapeutic Drugs. By Ashton L. Welsh, M.S., M.D., Assistant Professor of Dermatology and Syphilology, University of Cincinnati College of Medicine, Cincinnati, Ohio. Publication number 350, American Lecture Series, monograph in Bannerstone Division of American Lectures in Dermatology. Edited by Arthur C. Curtis, M.D., Chairman, Department of Dermatology and Syphilology, University of Michigan, Ann Arbor. Cloth. $4.75. Pp. 139. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

In a period of only five years tranquilizers have been produced and consumed at an alarming rate, probably exceeded in volume of total sales only by antibiotics and vitamins. A new language has been developed concurrently: ataraxic, normalizer, calmative, neuroleptic, psychic energizer, antiphobic, and phrenotropic are among the new terms constantly found in lay and medical literature. While in many instances these psychotherapeutic agents induce an improved mental state, they frequently produce undesirable subjective responses, toxic side-reactions, and objectionable effects when given with other drugs.

The principal groups of these drugs are the phenothiazines, the rauwolfia alkaloids and fractions, the substituted propanediols, the diphenylmethane derivatives, the ureides, and the amides. All of these categories contain drugs more familiar to practitioners under such popular names as Thorazine, Sparine, Compazine, Serpasil, Miltown, and Atarax. Each is listed in this useful book by generic as well as proprietary name, accompanied by details or its chemical formula, pharmacological action, administration and dosage, general and specific uses, toxic effects, and side-reactions. The listings are orderly and admirably arranged for quick reference. Specific dermatological uses, dermal reactions and allergic phenomena, cardiovascular complications, and side-effects on the central nervous system are stressed.

Many problems have arisen from the vast outpouring of tranquilizing drugs. When 30% of the prescriptions written in the United States contain one of these drugs, many physicians cannot be fully alert to the danger that artificially produced "peace of mind" may only drug mankind into hopeless inertia. The author is fully justified in his emphatic conclusion that "tranquilizing agents offer no substitute for accurate diagnosis or adequate medical supervision: they are adjuncts likely to displace, but never to replace some other forms of therapy." No physician should prescribe these drugs indiscriminately. This book, excellently produced, contains an extensive bibliography and an index.

A Textbook in Rorschach Test Diagnosis for Psychologists, Physicians and Teachers. By Ewald Bohm, Ph.D. Translated by Anne G. Beck, M.A., and Samuel J. Beck, Ph.D., Professorial Lecturer, University of Chicago, Chicago. Cloth. $7.75. Pp. 322. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

The Rorschach test has become, over the years, the major instrument of clinical psychologists engaged in psychodiagnostics. This volume brings to the United States, in translation from the German, much of the foreign literature previously available only in that language. It is a careful presentation of the author's views on the use of the test. While the author chose to present a step-by-step manual, taking the reader through each minute stage of administration, scoring, and interpretation, the completed volume is far from being a beginner's textbook. This is a highly sophisticated and complex presentation which will be welcomed by the initiate, an adjunct to other reading for the novice, and quite beyond the uninitiated. The language of the book is largely made up of "Rorschach vernacular" presented from the particular bias of the author and the translators, who frequently draw direct causal relationships between pathological states and specific Rorschach signs. The theoretical framework in which the author chose to make his interpretations is admirably presented.

In certain areas the author shows a broad acquaintance with the differing viewpoints expressed in the literature and indicates the need for caution in interpreting these factors. His discussion of intelligence and the use of the Rorschach test to measure this highly controversial facet of the patient is clear and precise, yet here and elsewhere throughout the book there is an almost too ready acceptance of opinion favoring the Rorschach test without evaluating opposite opinion. For example, in his discussion of organic psychoses he seems to accept without question the quotation "It may be considered a proven fact that the senility process is a reversing of the development process." Observers in gerontology, at least in the United States, hold that this still needs to be proved.

In the area of psychopathology the author is more questioning and more evidently alert to the complexities within the field. Here, while expressing himself with an unalleviated dogmatism, his

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

presentation is logical, precise, and well reasoned. The book is unlikely to be read widely outside the field for which it was written because of the amount of complicated personality evaluation within it. In its field, however, and certainly among those who share the author's Rorschach orientation, the book should soon become a standard textbook and reference work. While the medical practitioner may find it generally too complex, many psychologists should find new and interesting facets of psychodiagnostics clarified for them. As a highly specialized book on a subject that needs constant elaboration this should become a part of most reference shelves on the Rorschach test.

Leukemia. By William Dameshek, M.D., Professor of Medicine, Tufts University School of Medicine, Boston, and Frederick Gunz, M.D., Ph.D., Hematologist, Christchurch Hospital, Christchurch, New Zealand. Cloth. $15.75. Pp. 420, with 143 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W. C. 1, England, 1958.

This excellent book is the first comprehensive treatise on leukemia published in the past 20 years. It covers the entire field in detail and with a comprehensive bibliography, with chapters on etiology, classification, prevalence, symptoms, special features, prognosis, and treatment. The strongest parts of the book are the sections on the clinical aspects of the disease, which are discussed in detail with emphasis on the great variability of the diseases; their differences at various stages; their complications, both common and unusual; and the problems of diagnosis and differential diagnosis, which often offer difficulties. The fact that the findings in leukemia are not static but endlessly changing, offering a constant diagnostic and therapeutic challenge, is stressed. The chapter on treatment is comprehensive. Not only are general indications and contraindications for the various agents given but detailed discussion accompanies the explanation of the use, method of administration, and limitations of each therapeutic agent. The type is large and clear, and the photographs of clinical material, roentgenograms, tissues, marrow, and blood are uniformly excellent; but the colored illustrations, unfortunately, are highly diagrammatic. There are many excellent charts summarizing clinical and other data. Two minor criticisms might be raised. The first is of the emphasis on the "myeloproliferative" disorders and the attempt of the authors to develop or expand a unified system based on morphologic rather than etiological or dynamic grounds; the second is of the somewhat chatty and informal tone which creeps in and seems, at times, out of place. Students should find the book handy for reference; hematologists, for a comprehensive summary; and all others whose practices bring them in contact with leukemia, for a practical guide.

A Compendium of Research and Theory on Stuttering. By Charles F. Diehl, Ph.D., Professor of Psychology, Director, Speech Center, University of Kentucky, Lexington. Publication number 344, American Lecture Series, monograph in Bannerstone Division of American Lectures in Otolaryngology. Edited by Norton Canfield, M.D. Cloth. $9.75. Pp. 314. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1958.

The behavior complex called stuttering, whether it is a speech impediment, a psychological symptom, or a habit pattern, has received broad attention in both popular and scholarly literature. Books have been written expounding particular theories, detailing research, advising parents, elaborating self-cures, and explaining therapies for this condition. At times it appears that the reverse of Mark Twain's comments on the weather is true of stuttering. Everybody is not only talking about it but seemingly doing something about it, and yet like the weather it goes on and on. There seems to be the same number of stutterers (about 1% of the population) despite the work being done to alleviate the condition. This book reflects this widespread interest. It is truly, as the title implies, a compendium of research and theory. It was published because it was believed that a summary of what has been written in the field was needed. The book presents brief synopses, in an orderly fashion and almost without evaluation of either their worth or their importance, of what has been said, studied, discovered, and conjectured in print about stuttering. It offers no qualifications of the material, presenting for each study or theory the author's name, the title of his study, whether a research design was employed, what the study was about, and the conclusions reached. It is often unclear, in its conclusions, whether these are the findings of the researcher or whether they represent judgments made by the editor.

To any student of stuttering the book will save many hours of library study, but to anyone interested in self-help for stuttering it will provide only confusion, for no one approach is represented as being better than another. If widely read by stutterers the book may end by working a hardship on clinicians, for any reader will be impressed by the multiplicity of theories, the lack of agreement among researchers, and the comparative lack of acceptance within the field of any single approach. The book is easy to read and simply designed, and the research seems adequately summarized. Professional practitioners engaged in working with stutterers will undoubtedly want the book for their reference shelves, and speech therapists should find it useful in filling out the gaps in their own reading. The general medical practitioner, however, will find the book of little interest.

The Management of Fractures and Dislocations: An Atlas. Volumes I and II. By Anthony F. DePalma, M.D., Professor of Orthopedic Surgery, Jefferson Medical College, Philadelphia. Cloth. $35 per set of 2 volumes. Pp. 469; 471-960, with 1927 illustrations by Barbara B. Finneson and William A. Osburn. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

In this large atlas of fractures and their treatment the author has handled his subject well but not logically. With a little rearrangement all the fractures and dislocations of the upper extremities could have been placed in one volume, and those of the lower extremities in the other, but this was not done. This is not a serious criticism, because one would certainly buy both volumes in any case, and in spite of this the presentation of any fracture can be located easily. The book contains nearly 2,000 clear, distinct line drawings. Each drawing is accompanied by a brief description which would make the book of special value in the admitting department of a hospital. For some unaccountable reason, there is no description of the Leadbetter maneuvers for reduction of fractures of the neck of the femur. In the case of fractures of the ankle and leg there are no plates showing a pin or tongs in the os calcis to gain skeletal traction for the explosion type of fracture in the lower end of the tibia. Some rather terse comments, such as "don't abandon a pathological fracture" and "never use a tourniquet in open fractures," are especially commendable. Although all will not agree with the author's method, the book is easy reading and the illustrations are good.

Electrocardiography. By E. Grey Dimond, M.D. Director, Cardiovascular Laboratory, Professor of Medicine, University of Kansas Medical Center, Kansas City. Second edition. Cloth. Pp. 172, with illustrations. University of Kansas Medical Center, Rainbow Blvd. at 39th St., Kansas City 12, Kansas, 1958.

This book is especially designed for the beginner and is written in simple terms. The diagrams are also clear and so elementary that some readers might be annoyed at not being given credit for a higher level of intelligence, but the author, who has had many years of experience in teaching electrocardiography, has probably found that the average physician has forgotten even the most elementary principles of electrophysics. In a book of this sort the material must, for purposes of clarity, be presented in a dogmatic manner. In spite of this handicap the author has managed to give a remarkably accurate presentation of current concepts in electrocardiography in a practical manner. There are several references to other books on the subject. This is an ideal book for the general practitioner who is anxious to be introduced to electrocardiography.

A Symposium on the Evaluation of Drug Toxicity. Editors for Imperial Chemical Industries, Ltd. (Pharmaceuticals Division): A. L. Walpole, Ph.D., B.Sc., and A. Spinks, M.A., Ph.D., B.Sc. Cloth. $5.50. Pp. 138, with 58 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Place, London, W. 1, England, 1958.

This book presents the transcript of a symposium held at Alderley Park, Macclesfield, England, on Oct. 1, 1957, in conjunction with the opening of the new research laboratory of the Imperial Chemical Industries, Ltd. The skilled investigator, familiar with the methods of evaluation of drug toxicity, will find little of interest in this book, since most of the material appears to be somewhat elementary. The papers dealing with the discussion of the toxic action of drugs on the liver and on the bone marrow, by exception, become so involved that the average reader may find the text difficult. It is doubtful whether most readers of THE JOURNAL would care to add this book to their libraries.

Viral and Rickettsial Infections of Man. Edited by Thomas M. Rivers, M.D., and Frank L. Horsfall, Jr., M.D. Aided by grant from National Foundation. Third edition. Cloth. $8.50. Pp. 967, with 134 illustrations. J. B. Lippincott Company, E. Washington Sq., Philadelphia 5; 4865 Western Ave., Montreal 6; Pitman Medical Publishing Company, Ltd., 45 New Oxford St., London, W. C. 1, England, 1959.

The rapid growth and development of virology and rickettsiology amply justify the appearance of this new edition. It contains seven new chapters, and there are 14 new authors. The first 12 chapters are devoted to the more fundamental aspects of virology and rickettsiology and include discussions of the chemical and physical properties of viruses, the virus–host cell relation, interference, chemotherapy, the important techniques used in the propagation of viruses and Rickettsiae, the serologic reactions in viral and rickettsial infections, and the principles of epidemiology. In the rest of the book every important viral and rickettsial disease is considered in detail. The discussion of each infection includes something of its history, cause, symptoms, lesions, diagnosis, treatment, and control measures. The student, the clinician, and the investigator should find in this book all of the information available concerning viral and rickettsial diseases. If a particular technique or piece of information is not presented in detail, adequate references are usually provided at the end of each chapter. In spite of the fact that there are many contributors there is little if any reduplication of subject matter in the various sections. The editors hoped that this book would prove useful to physicians, teachers, and investigators, and this objective has been attained. No one who is interested in the general subject of viral and rickettsial diseases should fail to read this book.

QUESTIONS AND ANSWERS

CEREBRAL ARTERIOSCLEROSIS

To the Editor:—*Have any studies been made on the use of desoxyribonucleic acid or ribonucleic acid in the treatment of cerebral arteriosclerosis? Supposedly, some months ago, an article was published in the* American Journal of Psychiatry, *advocating its use.*

W. W. Brubaker, M.D., Annville, Pa.

Answer.—The correspondent apparently refers to a report by Cameron (*Am. J. Psychiat.* 114:943, 1958) in which the use of nucleic acid in aged patients with memory impairment is described. According to Cameron desoxyribonucleic acid and ribonucleic acid were given intravenously in doses of 100 to 500 mg. Ribonucleic acid was also given orally in daily doses of 10 to 20 Gm. In all 23 patients treated favorable results were noted. In one-half the results were good. The best results were obtained in those with severe memory deficits and marked confusion. Results were usually noted in four or five days. Intravenous injection appeared to be a better method than use of the oral route. Hyaluronidase was given intrathecally to some patients. It is hoped that effective and simple treatment will be available for aged patients with memory impairment, presumably so-called senile dementia or chronic brain syndrome. The report referred to is a preliminary one and lacks specific details in all of its aspects. Control data are wanting. Further study will be needed before this treatment can be routinely recommended.

STAPHYLOCOCCIC INFECTIONS

To the Editor:—*Would it be advisable to withhold one, or possibly two, antibiotics in a hospital of 200 beds to prevent severe staphylococcic infections? Should a surgeon with known active furuncles of such exposed portions as the face, neck, or hands, or one who is a carrier of staphylococci, be allowed to enter the operating room?*

M.D., Wisconsin.

Answer.—Many consider it advisable to withhold one or two antibiotics from general use. Erythromycin and oleandomycin are two that one staphylococcic infection committee recommended holding in reserve for use in proved resistant staphylococcic infections. Penicillin, streptomycin, tetracycline, chloramphenicol, and novobiocin are prescribed as indicated. Another group might feel it wise to withhold a different collection from general use. In most hospitals any person with obvious active furuncles is denied access to the operating suite. The question of staphylococcic carriers is a difficult one. One may have negative cultures one day and positive the next. Careful technique with adequate masks and frequent changes would seem the best answer.

MYELOGRAPHY AND DISKOGRAPHY

To the Editor:—*What risks are associated with myelography and diskography? Is a surgeon justified in obtaining a myelogram or diskogram to establish evidence of disease for medicolegal reasons, or are these procedures justified only to establish additional clinical evidence when symptoms are severe enough to demand surgery?*

William L. Minear, M.D.
Albuquerque, N. Mex.

Answer.—The risk of myelography consists primarily in the development of adhesive arachnoiditis after retention of the contrast medium. The degree of such arachnoiditis depends, to some extent, on how much contrast material is left in the spinal canal after the injection. Iodized oil tends to remain indefinitely in the dural sac, whereas iophendylate is absorbed gradually over a period of months or years. If the patient has leaned forward long enough, so that the contrast medium has flowed into the cranial cavity, the cranial subarachnoid spaces may be affected. There is some evidence that blood tends to emulsify the iodized oil and may add to the likelihood of producing arachnoiditis. Arachnoiditis may occur without myelography or surgery. Patients involved in litigation have symptoms ascribed to retained contrast medium more frequently than others. Arachnoiditis and radiculitis have not been reported after diskography. At least two cases of infection of the intervertebral disk have been described, in a few thousand diskograms.

In the case of a suspected intraspinal protrusion of an intervertebral disk, the diagnosis and indications for operation are usually primarily determined clinically. Myelography is generally indicated as a preoperative measure to confirm the clinical impression, to make a more exact localization, to seek the presence of multiple disks, and to exclude other conditions, such as neoplasm. Diskography has not

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

been widely accepted, and some of its early proponents have abandoned the procedure. This consultant agrees with the proponents of diskography that, after negative findings in the myelogram, diskography is to be preferred to a direct exploration, so that no operation is performed if the diskography shows normal findings. On the other hand, it would be of interest to know the frequency of derangement of an intravertebral disk in asymptomatic persons. When a myelogram, or diskogram, is recommended for medicolegal reasons only, the surgeon should emphasize the risks of the procedure and leave the decision to the patient. If the patient decides to request the procedure anyway, some surgeons refuse to carry it out for these reasons only but others may properly do so.

MEDICOLEGAL QUESTIONS

To the Editor:—*From the medicolegal point of view, is there any evidence that trauma or any extraneous cause may produce cancer, sarcoma, or leukemia or congenital, endocrine, or metabolic disease? In one case, a woman received a blow on the left breast in an automobile accident and within a year carcinoma of the left breast developed. In another patient, after contusion of the tibia a Ewing sarcoma developed in that bone. In an x-ray technician who developed leukemia, could overexposure to x-rays during the course of employment have been a causative factor? A pregnant woman was exposed to carbon monoxide fumes from a defective furnace, and her child was born with a cleft palate and intestinal abnormalities, requiring colostomy. Three siblings were normal, and there was no history of this condition in other members of the family. Did the carbon monoxide poisoning contribute to the development of these deformities? After an automobile accident in which there was severe emotional strain, a patient developed diabetes. Was the accident a precipitating cause of the diabetes? Another patient developed rheumatoid arthritis after a similar experience. Did the accident contribute to the development of the rheumatoid arthritis?*

William L. Minear, M.D.
Albuquerque, N. Mex.

Answer.—There is no evidence that a single episode of trauma ever produces cancer. There are cases reported in which repeated trauma seems to have played a role, and several reports have implicated exposure to x-ray therapy as a cause of leukemia and carcinoma of the thyroid gland. There are several hundred known carcinogens which can be extraneous causes of cancer. It would be difficult to relate carbon monoxide poisoning and congenital deformities or emotional strain and diabetes or rheumatoid arthritis.

HAZARDS OF SNUFF AND CHEWING TOBACCO

To the Editor:—*What are the possible harmful effects of the use of snuff and of chewing tobacco?* *M.D., Virginia.*

Answer.—Dygert (*New England J. Med.* 257:311, 1957) showed that snuff may be a source of the pathogens Pseudomonas aeruginosa and Proteus vulgaris. He reported a case of bronchitis in which the clinical and cultural findings showed that these organisms were pathogenically active. When the use of snuff was discontinued, the pathogens disappeared from the sputum. After a few weeks these organisms reappeared in the sputum, and the patient admitted that he had been chewing cut plug tobacco. When he stopped chewing tobacco, the organisms disappeared again.

Chinachoti and Tangchai (*Dis. Chest* 32:687, 1957) reported pulmonary alveolar microlithiasis in a patient who had been a heavy user of snuff for 23 years. They expressed the view that the pulmonary lesions found at autopsy were associated with the inhalation of snuff, which is composed of tobacco and earthy material. The low content of silica and the nature of the pulmonary lesions excluded silicosis.

The results of chewing tobacco are not well defined. One explanation is that the nicotine in smoke is in a more finely divided state than it is in tobacco juice derived from chewing tobacco and thus it is absorbed more easily from smoke than from tobacco juice through the oral mucosa; therefore, the concentration in the blood, derived from tobacco juice, may be less. Biebl and co-workers (*Am. J. Physiol.* 100:167, 1932) reported that when nicotine is absorbed from the gastrointestinal tract, it is detoxified by the liver before it reaches the general circulation.

SHOULDER-ARM SYNDROME

To the Editor:—*After an acute coronary occlusion which seems to have healed well, a patient had no sequelae except severe left shoulder and arm syndrome which failed to respond to treatment. X-ray therapy, cortisone injections, methylprednisolone (Medrol), vitamin B complex, dextropropoxyphene hydrochloride (Darvon) compound, salicylates, aspirin, and vitamin* B_{12} *were tried without benefit. How long may this shoulder-arm syndrome be expected to last, what is its cause, and is there any other treatment which might give relief?* *M.D., New Jersey.*

Answer.—The pain fibers from the fourth cervical segment to the second thoracic segment overlap in producing painful arm and shoulder syndromes in connection with cardiac pain of a referred type. Because of this, many patients with coronary insufficiency, angina pectoris, and myocardial infarction have referred pain in the left shoulder. This pain tends to limit the motion of the left shoulder. The fixation of the shoulder and lack of motion produce a synovitis of the joint which further restricts shoulder motion. This, in turn, produces an atrophy of disuse, particularly of the deltoid muscle. The patient suffering from any of the above-mentioned conditions should keep his hands above his head for 10 or 15 minutes four or five times daily. Those who do this seem to have no trouble with the so-called cardiac arthropathies. Free extension of the shoulder in the lateral and perpendicular positions will free these adhesions. Sometimes this must be done with the patient under anesthesia to produce full abduction. Maintenance of this free position plus regular exercise usually results in a normally functioning shoulder. Incidentally, it has often required more time to cure these arthropathies than the myocardial infarction.

IDIOPATHIC HYPOGLYCEMIA

To THE EDITOR:—*Are there any ill-effects from a continued low-carbohydrate diet containing 100 to 150 Gm. of protein per day in a patient with idiopathic hypoglycemia? Would it be likely to cause an osteoarthritis or aggravate a preexisting one?* *M.D., California.*

ANSWER.—In a healthy person wide ranges in dietary composition are tolerated with no apparent ill-effects. A diet low in carbohydrate and with 150 Gm. of protein should not cause or aggravate osteoarthritis. The low-carbohydrate high-protein diet designed to render a steady support to blood sugar by gluconeogenesis, rather than sudden rises as with carbohydrate, has enjoyed a vogue in the treatment of functional hypoglycemia, but while this was an interesting concept, such treatment frequently failed. The most popular current concept is that functional hypoglycemia is a psychosomatic disorder and that it frequently responds to a sympathetic ear and reassurance. Osteoarthritis to date has been linked with trauma and the aging process. Its cause and pathogenesis are unknown. There is no evidence that it is related to carbohydrate metabolism or changes in the diet. This statement does not apply to such other forms of arthritis as gout.

ORTHOPEDIC TESTS

To THE EDITOR:—*Please explain the following orthopedic tests: (1) Nachlas, (2) Yeoman, (3) Lasègue, and (4) Viets.* *M.D., Louisiana.*

ANSWER.—In the Nachlas test the patient is placed prone on a hard table and the knee is flexed by the examiner. If the result is positive, the patient has pain in the sacroiliac joint, lumbosacral joints, and down the anterior and posterior aspects of the thigh and calf. The rectus femoris tightens up and extends the pelvis and spine, thus causing pain, if there is a lesion in the sacroiliac or lumbosacral area.

The Yeoman sign is not a test but a sign. Yeoman stated that arthritis of the sacroiliac joint caused sciatic pain in 36 of 100 patients with sciatica so that it actually would be determined by reading the roentgenograms. The symptoms are caused by a periarthritis of the anterior ligaments of the sacrum, the piriformis muscle, and radicals of the sciatic nerve.

The Lasègue test consists of reproducing the pain when the patient is flat on his back with the leg flexed and knee extended. It was described as a test for muscle spasm in the hamstring muscles. All three of these tests were described before the exact lesion being tested for was known, and varied explanations of the cause of the positive test were postulated, all of which were wrong. They are interesting historically but of questionable practical value if their original interpretations are to be held.

The Viets test is another example of the absurdity of using eponyms for tests. It is a test known by its practical value but not by this name. It is the neostigmine test for myasthenia gravis and consists of the injection of 1.5 mg. of neostigmine methylsulfate and 0.6 mg. of atropine sulfate per 150 lb. (68 kg.) of body weight. A positive result is judged clinically by an increase in the muscle strength and a clearing of the toxis.

IDIOPATHIC HEMOCHROMATOSIS

To THE EDITOR:—*In the person with idiopathic hemochromatosis what results may be expected from a determination of serum iron level and serum iron binding capacity? If these are normal, is further diagnostic work indicated, such as a liver biopsy or radioactive iron study? What is the best treatment?*

Marvin Garrell, M.D., Fairfield, Conn.

ANSWER.—The normal body weighing 70 kg. (155 lb.) contains 4 or 5 Gm. of iron. In idiopathic hemochromatosis there may be 25 to 50 Gm., and the serum iron level is usually elevated. Normally, the values are in the range of 100 to 150 mcg. per 100 cc. In idiopathic hemochromatosis the serum iron level may approach 300 mcg. per 100 cc.; but as the disease and the consequent liver damage progress, the plasma protein level may fall, and with it the serum iron level. Hence, more important than the serum iron level is the degree of saturation of the iron-binding globulin, transferrin (siderophylin). Normally this is only about 40% saturated, and while the normal serum iron level is 120 mcg. per 100 cc., the siderophylin can bind

300 to 400 mcg. per 100 cc. when it is completely saturated. In idiopathic hemochromatosis and transfusion hemosiderosis, the saturation of the iron-binding globulin approaches 100%.

If the serum iron level is normal and saturation of serum for iron is less than 50%, then hemochromatosis can be excluded and a liver biopsy is not necessary. It might be included as a diagnostic tool for other causes of cirrhosis. Radioactive iron is a research tool and was used to demonstrate that the defect in hemochromatosis is an increased absorption of iron from the gastrointestinal tract.

The best treatment for hemochromatosis depends on early diagnosis before liver damage has occurred, and then removal of the iron. For all practical purposes the excretion of iron is negligible, and to date the best method for the removal of iron has been repeated small phlebotomies, 250 to 500 cc. every three to six weeks. A 500-cc. phlebotomy removes 250 mg. of iron. The average diet contains 10 to 20 mg. of iron, of which less than 10% is normally absorbed. For this daily absorption of 1 or 2 mg., about 0.8 mg. is lost per day in desquamated cells, sweat, and urine; hence phlebotomy removes a significant amount of iron.

CHEMICAL BURNS OF RESPIRATORY TRACT

To the Editor:—*A 3-year-old boy ingested an indeterminate amount of ammonium thioglycolate (a home permanent neutralizer). Immediately after ingestion of it, the boy gagged, coughed, and vomited; he was cyanotic for three or four days. About two weeks later laryngoscopy revealed an inflammatory reaction of the larynx, trachea, and bronchi. About one year after ingestion of the poison he developed thinning and atrophy of the tongue. His voice is squeaky, and he has some hoarseness when he talks loudly. When he cries he sometimes has laryngeal stridor. What is the expected end-result of this scarring of the tongue and larynx?*

Howard Hansen, M.D., Baton Rouge, La.

Answer.—About a year ago, potassium bromate was being used as a neutralizer, but this was discontinued because of two or three reported deaths from the solution, and sodium perborate is now used as a neutralizer. The thioglycolate mentioned is found in the wave solution, but the caustic effect of this material has not been determined. The solution ingested caused a definite burn of the larynx and has apparently resulted in some laryngeal stenosis. It is unlikely that the thinning of the mucosa of the tongue would have any serious effect either in the immediate or distant future. It may be assumed that the patient had some loss of mucosa in the laryngeal area and as a result has obtained a fusion of the anterior commissure which has resulted in the high-pitched squeaky voice and hoarseness; it would also cause some stridor on breathing after unusual exertion. Since it has been one year since the accident, it is unlikely that the condition will progress beyond its present stage, and, as the child grows older, the size of the larynx would be expected to increase with his general growth, possibly not proportionately, but still sufficiently to allow him to avoid respiratory difficulty. The course of the condition should be followed with direct laryngoscopic visualization, first, to determine the exact condition of the larynx and, second, to have a standard for comparison in subsequent examinations.

MUSCLE REEDUCATION

To the Editor:—*I once attended a meeting at which Sister Kenny described her method of treating patients with paralytic poliomyelitis. She stressed the value of awareness or incentive on the part of the patient as the paralyzed muscles were passively put through their functional range of motion by the attendant after the hot packs had been used. She applied a special term, which I cannot recall, to this mental effort by the patient. Was this idea of conscious effort to move a paralyzed part during the passive exercise ever accepted by the medical profession?*

M.D., California.

Answer.—The Kenny method of muscle reeducation is divided into three phases. The first phase is tendon stimulation. This is an attempt to produce proprioceptive reflexes by passive motion of the joints normally moved by the affected muscles. It is done by several techniques, all of which involve stimulation of sensory proprioceptive endings to produce motor effects, and it is strictly a reflex action.

The second phase is restoration of mental awareness. This phase is probably the one mentioned in the question. In this technique the attempt is made to make the patient aware of the function of the muscle by using every type of sensory stimulation available. The normal motor pattern is reproduced by passive motion which involves proprioceptive stimuli. The skin is stroked over the insertion of the muscle to utilize tactile stimuli. The origin, insertion, and action of the muscle is described to the patient to provide auditory stimuli. The patient is allowed to watch the motion being performed passively to supply visual stimuli. All of these procedures are performed without the patient making any attempt at active motion. Fundamentally it is an attempt to reeducate the sensory side of the motor pattern.

The third phase is restoration of muscle function. At this time the patient first attempts to move the part voluntarily with assistance. Great care is taken to avoid substitution of other muscles in the motor pattern and to avoid tiring the patient during this reeducation process. As the patient develops more power and coordination he is allowed to do more for himself until he is able to perform the motion independently. This phase is an attempt to reeducate the motor side of the motor pattern. The technique is described more fully in the chapter Exercise in Poliomyelitis in "Therapeutic Exercise," volume 3 of the Physical Medicine Library, published by Elizabeth Licht, New Haven, Conn. It is used with some modifications in many poliomyelitis centers.

CHLORAMINES IN SWIMMING POOL

To the Editor:—*The water in a swimming pool is treated with chlorine soda ash and filtered through pressure sand filters. The pH of the water is maintained between 7.8 and 8.0, and the chlorine content varies from 0.8 to 1.0 ppm. When water is treated with chlorine, one of the by-products is nitrogen trichloride, an insoluble gas that tends to lay close to the water surface. This gas is irritating to the eyes of the varsity swimmers, who are taught to skim the surface, swimming with their eyes open. There have been no complaints from the womens' physical education class or other swimmers of the pool. Sufficient ventilation to remove this gas would be prohibitive not only in terms of cost of ventilation equipment but in terms of heating the air supply. What measures will prevent the eyes from burning due to exposure to this water?*

M.D., Nebraska.

Answer.—The analysis made of the reasons for the difficulties being experienced is not factual. In pool waters which contain ammonia, the addition of chlorine will cause the formation of chloramines. The particular chloramine depends on the pH of the pool water. At the pH level being maintained in this particular pool there is little likelihood that the trichloramine nitrogen trichloride will be formed. Trichloramine production would require a pH of about 4.5 to 5.0.

Studies on this problem indicate, however, that the monochloramines and dichloramines are eye irritants and may be responsible for the difficulties being experienced in this particular pool. Studies have indicated further that by the application of break-point chlorination, the chloramines can be eliminated with the formation of nitrogen and the oxides of nitrogen. This requires the maintenance of a pH of about 8.0 with a free residual chlorine of 2 to 3 ppm. A number of articles have been written on this subject. One article by Eric W. Mood appeared in the *American Journal of Public Health* (43:1258-1264 [Oct.] 1953). Mr. Mood has been highly successful in eliminating eye irritation among the varsity swimmers at Yale University by the application of this type of treatment to their pool water. Many others have confirmed his findings.

SPONTANEOUS ABORTION

To the Editor:—*Please comment on proper hospital routines for patients who have had a spontaneous abortion. What routine orders should be given to the nursing staff to prevent pelvic infection? May patients safely be placed in a room or ward with other patients with infectious diseases, such as pelvic inflammatory disease?*

M.D., Missouri.

Answer.—Most patients who have had a spontaneous abortion experience an uneventful afebrile convalescence, but it is not always possible to determine whether such persons have been subjected to manipulations to induce the abortion, with the increased likelihood of puerperal infection. A patient who has had an abortion should not be placed in the same room with a recently delivered mother nor should she be exposed to a gynecologic patient with subacute or acute pelvic inflammation. The patient who is febrile on admission, prior to the spontaneous abortion, or who develops fever should be isolated outside the clean maternity sections. She should be treated in the same way as a delivered mother who develops puerperal infection.

POSTHERPETIC PAIN

To the Editor:—*About five years ago, an 82-year-old woman, after an attack of herpes zoster at the level of the hemithorax and the right arm, developed a persistent pain in the right arm. At times her pains become so intense that she had to use ketobemidone for relief. The skin of the inner side of her arm and forearm is hypersensitive, wrinkled, and dry, and the hand has remained edematous for nearly two years, not permitting any movement of the fingers because of the pain. Roentgenograms of the hand showed ankylosis of practically all joints. Since the onset, sodium salicylate, piperazine, ACTH, cortisone, vitamin B_{12}, and procaine have been used but without relief. Can you suggest any treatment for this patient? What case fatality rate attends surgical treatment?*

Harry Kalenscher, M.D., Flushing, N. Y.

Answer.—Postherpetic pain is always difficult to treat and sometimes cannot be affected by any known treatment. In some patients it responds well to section of the peripheral nerve or relevant posterior nerve roots. In others, there has been some response to stilbamidine and large doses of vitamin B. The age of the patient in question seems to contraindicate radical surgery, yet local block of the thoracic nerve concerned may provide relief.

If regional block with procaine gives relief, one might consider a simple section of the thoracic nerve with the patient under local anesthesia. Sometimes such sections at the periphery cure or greatly ameliorate the pain. If this procedure fails, a posterior root section might be considered. The morbidity and mortality with such a procedure is low, although it would be somewhat higher in an elderly person. In competent hands, the procedure is short and may even be performed with the patient under local anesthesia, if general anesthesia is contraindicated.

SERUM AMYLASE

To the Editor:—*A patient has a consistently elevated serum amylase level (175 to 200 units per 100 ml.). The normal for the laboratory is up to 110. I am unable to find a cause for this. He complains of pain in the left parotid gland, which at times appears to be slightly enlarged, but he has not been febrile and has no manifest parotitis. Are there other causes of elevated serum amylase level besides inflammation of the pancreas and parotid gland?*

M.D., Illinois.

Answer.—Moderate elevations of serum amylase, that is, to levels from 200 to 700 units per 100 ml., may be found in such conditions as peptic ulcers penetrating or perforating into the pancreas, calculous obstruction of the salivary duct, renal insufficiency due to chronic or acute glomerulonephritis, chronic pancreatitis with a relapse involving previously unaffected tissue, and sometimes carcinoma of the pancreas. Apparently this patient has no renal insufficiency. Since he does complain of pain in the left parotid gland and shows occasional enlargement of this gland, the possibility of a small calculous obstruction of the salivary duct might be considered first.

SIMPLE CHRONIC ANEMIA

To the Editor:—*In reply to the question on simple chronic anemia, which appeared in* The Journal, *Sept. 13, 1958, page 227, the consultant stated, "The anemia will not respond to the administration of iron, vitamin B_{12}, folic acid, or any of the 'shotgun' antianemic preparations which, unfortunately, flood the pharmaceutical market." This appears to be an overstatement of facts. It may be asked on what basis the consultant concluded that none of these hematinics or a combination thereof would help the patient. In tropical countries, it is known that the iron taken in food often is not absorbed. Much of what is absorbed is excreted in the perspiration, and there are other nutritional deficiencies that are amenable to one or more of these hematinics or to a combination thereof, as in dimorphic anemias. Horrigan and co-workers* (Am. J. Med. 22:99, 1957) *found that in hyperferricemia none of the other hematinics helped until liver was given orally.*

K. S. Dharadhar, M.D.
P. O. Box No. 229
Bombay 1, India

The above comment was referred to the consultant who answered the original question, and his reply follows.—Ed.

To the Editor:—*The statement that none of these hematinics or a combination thereof would help the patient was based on the assumption, justified from the data provided, that if the patient had anemia at all it was of the simple chronic variety. This subject is beautifully discussed and documented, in terms of pathogenesis and treatment, by Wintrobe (Clinical Hematology, ed. 4, Philadelphia, Lea & Febiger, pp. 581-588). The original answer is entirely consistent with the views expressed by Wintrobe. The comment states that in tropical countries the iron taken in food often is not absorbed. Though this consultant has studied iron metabolism for years and is familiar with most of the literature on iron absorption, no studies have been seen that justify that statement. They would depend on careful balance studies or measurements with radioactive iron. If the commenting physician knows of such a published work, a reference to it would be appreciated. The question is hardy applicable to the specific case being discussed, however, since there was no evidence of iron deficiency.*

The comment further states that a lot of iron is excreted in the perspiration. Foy and Kondi offer evidence to indicate that there is a dermal loss of iron in the tropics from desquamation of epithelial cells (not in perspiration, per se), but even their work has not entirely eliminated iron contamination from the environment. Even if one accepts their work at face value, the fact remains that there is no evidence to indicate that persons with simple chronic anemia in the United States are iron-deficient or will respond to the administration of iron. The correspondent states that there are other nutritional deficiencies that are amenable to one or more of these agents or sometimes to a combination thereof as in dimorphic anemias. This is true, as Wintrobe also states, but the values given in the original inquiry would not be low enough for a dimorphic anemia. Even though one may have mild degrees of anemia in various nutritional disturbances, such as thiamine deficiency and pellagra, the use of a shotgun preparation is still not justified. The observations of Horrigan and co-workers are accepted without reservation. The situation must, however, be rare. This consultant knows of no cases other than those reported by him or to which he refers.